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WEATHER AND RESISTANCE IN PULMONARY TUBERCULOSIS[1]

PART I

W. F. PETERSEN, J. S. HOWE AND M. E. MILLIKEN

INTRODUCTION

Of the well defined clinical phenomena in tuberculosis, none are so evident as the seasonal influences first described by Hippocrates (1): the onset or activation in the late winter and spring, the summer quiescence, the autumnal exacerbation. Obviously the mechanisms of resistance must be closely related to seasonal change in the physiological and immunological state of the subject.

This interesting interrelation one of us has previously described (with Levinson) (2, 3) and documented by integrative studies that related the change in the environment with the biochemical and clinical changes in patients (4).

In the cases that are here presented we have continued and intensified the detailed analysis in 6 tuberculous patients of different types, adding blood cultures, quantitative tuberculin reactions, etc. to the day-by-day investigations carried on over long periods of time. In addition, observations were made on the effect of continued alkalinization.

Inasmuch as the detailed protocols would be too extensive to permit publication for all 6 cases, only that of the first patient is included. So, too, comments concerning all the day-by-day variations are impossible for the same reason, and we have limited ourselves to the selection of a few episodes in each graph to illustrate certain characteristic features. The techniques employed have been previously described (5).

The metabolic status of the human (and mammals in general) domiciled in the region of the cyclonic atmospheric circulation is constantly pendulating between poles of increasing and decreasing activity. The passage of each polar air mass is first associated with a transient "stop" phase, during which time there exists a relative sympathicotonia, the

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blood pressure levels are increased, respiratory rates and pulse rates decrease, anabolism is accentuated, sugar is mobilized, cell membranes are less permeable, there is relative dehydration. In the tuberculous patient there is a lessening of the output of sputum. This phase is succeeded by a compensating "go" phase when metabolism is increased, the blood pressures fall, temperature, pulse rate and respiratory rate are increased, leucocytosis is evident, tissues begin to be hydrated, membranes are more permeable, etc.

Obviously activation of tuberculous processes, whether considered from the histopathological concept, from the point of view of the clinical findings or with consideration of toxic and allergic phenomena, will tend to be retarded by the first stage and accentuated by the second stage. Progression of the disease, finding clinical expression in pathological extension and bacterial dissemination, or the opposite, namely, increased resistance to the disease, will in our region of the world constantly pendulate between the two poles of the metabolic state. In the late winter and spring the "go" phase or the "COD phase" (C—catabolism, O—oxidation, D—dilatation of vessels) is enhanced, largely the end-result of biological exhaustion of reserves, which follows as a result of the repeated passage of polar air masses. The organism becomes relatively acid, the blood pressure is low, bone marrow is exhausted, hydration is accentuated, tissue turgor and tone are diminished.

In the summer and autumn this trend is reversed, with corresponding clinical effects. Needless to say, in the environmental effects which condition the organism, not only the weather, that is, the air mass in which the patient exists, is to be considered, but all factors accessory thereto. Sunlight, atmospheric turbulence or quiescence, the seasonal changes in diet, increased or lessened intercurrent infections—these and many more play a rôle, but we are here concerned largely with the changes in the cyclonic circulation of the atmosphere and it is this feature which will be stressed in our discussion.

It is not possible to enter into a detailed discussion of the atmospheric circulation (6). We would merely call attention to the continuous alternation of warm (tropical) air masses, characteristic of the cyclone, with cold (polar) air masses, characteristic of the anticyclone. Particularly the passage of interfaces of these diametrically opposite air masses, representing contact zones of great instability, requiring rapid adjustment on the part of the human organism, are periods of great strain.

Obviously, the greater the difference in the character of the air masses,

the greater the frequency and rapidity of the passage of such interfaces or "fronts," the greater the strain on the mechanisms of adjustment.

Such adjustments become evident in the chemical as well as physiological alterations and in turn in the clinical symptomatology, because any focus of diseased or dysfunctioning tissue will present a region of undue sensitivity. Seasonal effects represent the accumulation of weather effects, they are summation phenomena, and because of this, seemingly minor environmental alterations may, at critical times, precipitate portentous clinical effects that are seemingly quite out of keeping with the relative insignificance of the change in the air mass. The assumption, therefore, that weather effects on the normal or tuberculous organism are simple, or that the same environmental effect must always bring about a like clinical effect or that a simple statistical analysis will be adequate to determine whether or not we are dealing with the meteorological effect, is not true. No meteorological situation is ever repeated and the organic base line on which it is effective is never the same. Under the circumstances every individual reaction and every individual patient presents a separate problem and it is for this reason that we have approached the subject from the point of view of a painstaking and long continued study of the individual case. Our conclusions, however, are adequately buttressed by statistical treatment of simpler meteoro-organic interrelations.

With this as an introduction the reader is requested to survey the graphic material from the point of view of observing the effect on the sick organism as it seeks to maintain an unstable equilibrium in an unstable environment, an environment which initiates physiological alterations that may at one time be harmful, at another beneficial—the outcome depending on habitus and nutrition, on inherited and acquired resistance, on age and sex, on dose and virulency of the infecting organism as well as a great number of other factors that may tip the scale in one direction or the other.

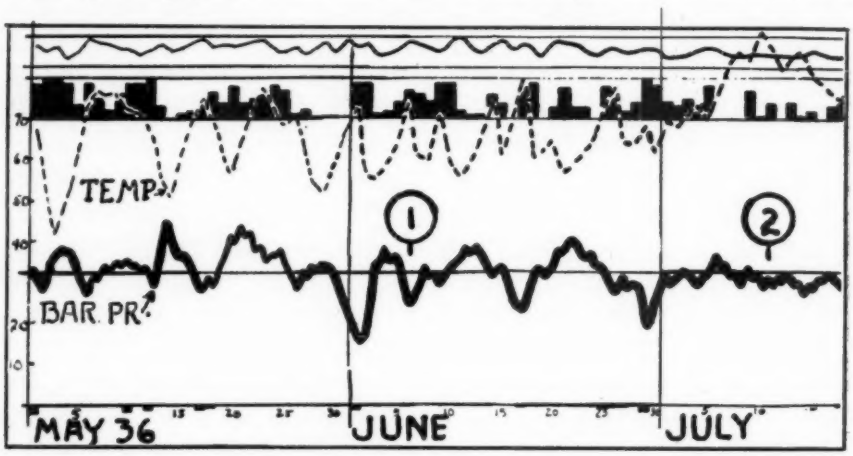
TUBERCULOSIS SUBJECT 1—FAR ADVANCED FATAL CASE

The first patient, W. K., a white male, twenty-three years of age, was studied from the end of August, 1936 to the time of his death on November 17, 1936.

Clinical History

In February, 1931 the patient had an episode which he considered a severe cold in his chest. His symptoms were pain in the chest bilaterally, a severe

productive cough and fever. He remained in bed for one week after which he returned to work as a painter. Weakness and fatigue were noted for two weeks after he returned to work, but he made a good recovery and had no further symptoms until June, 1936 (during the week of June 6 to 13) (episode (1), text figure 1) when he first noticed a persistent productive cough, marked fatigue and perspiration with very little exertion. He continued to work until July 11, when he consulted a physician (episode (2), text figure 1). During this period of four to five weeks he lost 25 pounds in weight and noticed some dyspnoea on slight exertion. From July 11 to August 22, he was treated at home by two physicians but continued to lose weight and to run a fever of



TEXT FIG. 1. Meteorogram for the period of activation recorded in the history of tuberculosis subject 1 as episodes (1) and (2). In the meteorogram the upper curve indicates the wind velocity, the black columns cloudiness, the dotted line daily mean temperature, the heavy curve the barometric pressure. Precipitation is indicated under the date line by black columns.

(1) Activation phenomena most pronounced.

(2) Activation phenomena accentuated and physician consulted.

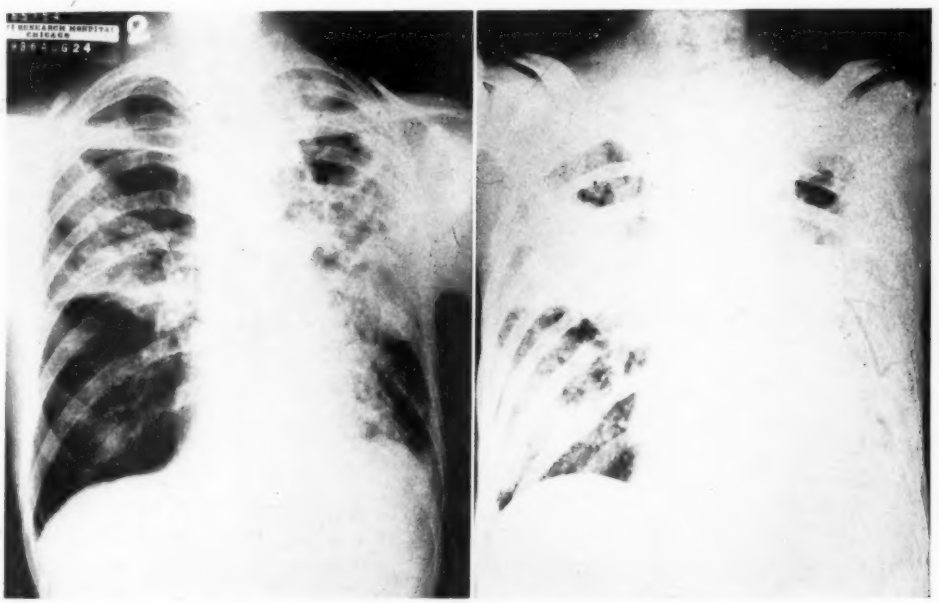
101° to 102° F. daily. He was admitted to the Research Hospital on August 22, 1936.

In the past history he had chicken pox and frequent tonsillitis as a child. The family history was apparently negative and there was no record of tuberculosis in the family. He had used no alcohol but smoked approximately one package of cigarettes a day.

Physical examination revealed a fairly well developed but poorly nourished young male who appeared quite ill. The lips were bright and red, there were some carious teeth and the tonsils and pharynx were injected. The chest was long and slender, the ribs prominent, chest expansion was normal on the right side but decreased on the left. A dull percussion note was obtained on the

right side anteriorly and posteriorly from the level of the fourth thoracic vertebra downward. Breath sounds were absent and bubbling râles were heard posteriorly and laterally.

The heart borders were within normal limits and the tones were regular, the rate approximately 110 per minute. Clinical impression was that of pulmonary tuberculosis, and laboratory examination of the sputum revealed a large number of acid-fast bacilli. The Wassermann and Kahn tests were negative, as was the urine. Haemoglobin was 7.8 g., red blood corpuscles 3,800,000.



ROENTGENOGRAM 1. (left) August 24, 1936
ROENTGENOGRAM 2. (right) October 13, 1936

Roentgenological examination of the chest made on August 24, 1936, (roentgenogram 1) showed irregular increased density over the lower part of the right upper lobe with radiolucent areas within same. The density was sharply outlined below in the region of the interlobar fissure. A large radiolucent area was present above it without lung markings, suggestive of a cavity. On the left side there was elevation of the diaphragm. Irregular densities were present throughout the lung extending into the parenchyma from the hilum region with a localized radiolucent area below the left clavicle. The mediastinal structures were displaced toward the left. Findings were consistent with old fibroid tuberculosis with cavitation.

Examination made October 13, 1936 (roentgenogram 2) showed extension

of process with involvement of right lower lobe in addition to findings noted on previous examination.

The Weather at the Time of Onset

The record has indicated that the onset of the disease occurred during February, 1931. It was not, however, until June, 1936 that findings indicative of tuberculosis became evident. Rather interesting in this connection is the fact that the winter of 1936 had been unusually cold in Chicago, with subzero temperatures existing through the latter part of January and the first of February. Activation apparently occurred during the week of June 6 **(1).**

We turn to a meteorogram (text figure 1) to illustrate the meteorological situation at this time. This meteorogram illustrates the following changes:

The uppermost curve is that of the wind velocity of the day, the black columns indicate the degree of cloudiness in terms of 100 per cent, the dotted line the daily mean temperature, the heavy line barometric pressure. Below the date line precipitation is indicated by the black bars.

The presumptive date of clinical onset is indicated by the circle **(1).** We note that barometric pressures had been usually low on the 1st and 2nd of June, at which time there was precipitation; this was followed by a considerable increase in barometric pressure with the passage of a cold air mass. The magnitude of the change in barometric pressure would indicate the possible change in the biological status of the individual subjected to this environment, and we have every reason to believe that vascular spasm, associated with anoxia, which in turn would have been followed by an increase in acidity, was associated with this event. All this would have been of material moment in bringing about lessening of tissue resistance and spreading of tuberculous involvement. At the next barometric low, when this trend would have reached its maximum, illness began.

Symptomatic accentuation must have followed because by July 11 he was forced to consult a physician **(2).** The reader will observe that this date represents an environmental accentuation of possible strain because we had the highest temperatures of the year. Blood pressures would have been low and fatigue phenomena would have been accentuated. (For actual biometeorograms of tuberculous patients observed during this time see cases 2 and 4.)

The Biometeorogram

We first examine the graph of subject 1 extending from August 25, 1936 to November 17, 1936, when the patient died (text figure 2).

A meteorogram **(R)** extended across the top of the graph contains the following:

The dotted line indicates the daily mean temperatures, which were in the nineties at the beginning of the observations. The autumnal decline follows in a series of steps to the time of the death of the patient.

The barometric pressure is indicated by the heavy black line, with a horizontal line through it to indicate the level of 30 inches.

The degree of cloudiness is indicated by the black bars extending across the upper portion of the curve; wind velocity is indicated by the topmost curve; the amount of precipitation is indicated by black bars extended down from the date line.

The curves at **(S)** reveal the changes in the blood count. Beginning at the bottom, these consist of the curve of the total leucocyte count, then above this is indicated the daily differential, with eosinophils indicated in the black columns. Above this, the percentages of immature forms of polymorphonuclear leucocytes are indicated and the uppermost curve of this group presents the percentage of polymorphonuclear leucocytes.

At **(T)** the curve indicates the methylene-blue disappearance time. This is the time (in hours) for complete disappearance of a standard quantity of methylene-blue injected intracutaneously. Reduction in time is an indication of lessened oxidation and, in general, occurs with increase in blood pressure.

The curves at **(U)** are those of the respiratory rate and the pulse rate; the respiratory rate indicated by a black curve, the pulse rate by a white curve.

At **(V)** the black field indicates the blood pressure, the upper margin representing the systolic blood pressure, the lower the diastolic blood pressure.

At **(W)** is the curve of the daily maximal and minimal temperature of the patient.

At **(X)** is the weekly weight curve.

At **(Y)** is the quantitative tuberculin reaction (7).

The subjective clinical record of the patient follows:

Clinical Notes

	October, 1936		October, 1936	
(1)	6	Tired	10	Feels better
	7	Poor night	11	Feels better
	8	Poor night; abdomen tender	(2) 12	Chest pain
	9	Tired	13	Drowsy
			14	

October, 1936		
	15	
(3)	16	Chest pain
	17	Chest pain
	18	
(4)	19	Chest pain; slept poorly
	20	Dyspnoea; slept poorly
(5)	21	Cough worse
	22	Chest pain
	23	Hoarseness
	24	Sore throat
	25	
	26	
(6)	27	Poor night
	28	Chills; weakness; poor night
	29	Sore throat; chest pain
	30	Abdominal pain; chest pain; cyanosis
	31	
November, 1936		
(7)	4	Chest pain
	5	
	6	
	7	Drowsy
(8)	8	Poor night; chilly
	9	Dyspnoea; cyanosis; weakness
	10	
	11	Tired; weak; poor appetite
	12	Tired
	13	
(9)	14	Flushed; cyanosis
	15	
(10)	16	Dyspnoea; cyanosis; confused
	17	Expired

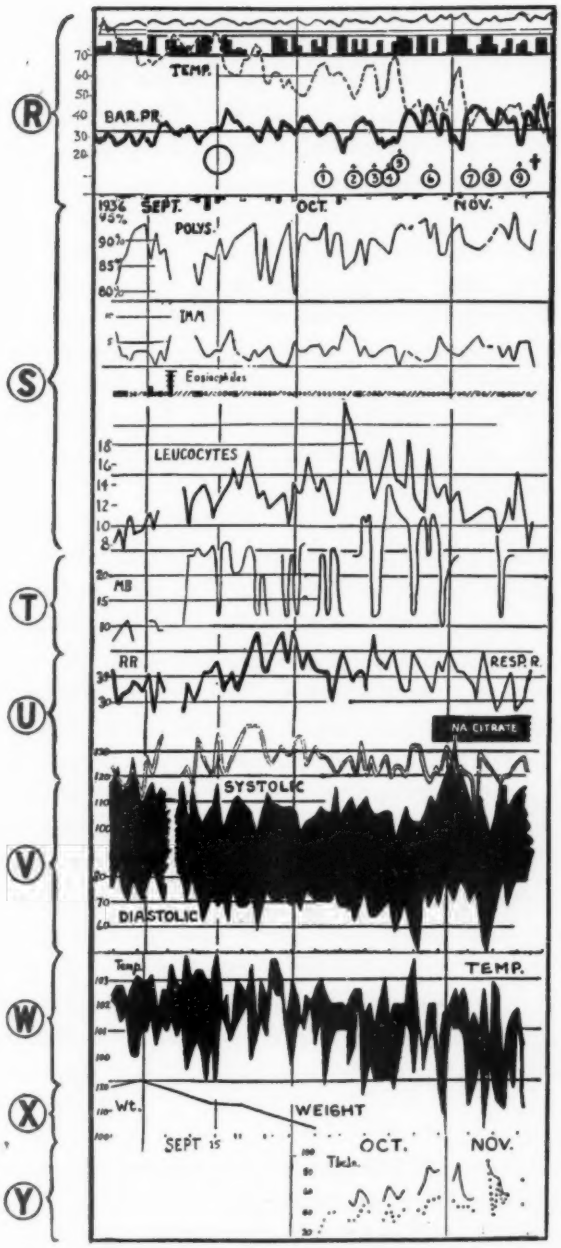
These episodes have been marked by circled numbers **(1)** to **(9)** and these are repeated just below the line of the barograph in the meteorogram. The death of the patient is indicated by a cross. Sodium citrate was administered in doses of 5 grains three times a day from October 29, 1936. This is indicated by the black bar at **(U)**.

In this first graph we would merely have the reader establish general familiarity with the methods used and the course of the observation as they relate to the weather and we shall therefore limit the discussion to the simplest of associations.

The weather of the period is one of strain for the tuberculous patient because a series of impacts, that is, cold, each result in a periodic increase in blood pressure (vasoconstriction) and with this a relative anoxia in large areas of the body. As a result, a liberation of capillary active substances follows, which ultimately lessens the resistance of the patient in step-like and progressive fashion, reflecting the step-like lowering of environmental temperatures. Each period of passing cold actually involves an undue energy demand.

We note first that the environmental temperatures were highest at the beginning of the period of observation. The leucocyte level was relatively low. Eosinophils were still present, that is, the bone marrow was not fatigued. The blood pressure levels were normal **(V)**, but the respiratory rate was increased **(U)**. Weight had not yet begun to diminish **(X)**.

For the next two weeks the environmental temperatures declined and



TEXT FIG. 2. Biometeorogram of tuberculosis subject 1. August to November, 1936. See text for detailed discussion.

a barometric crest on the 3rd, 4th and 5th of September is definitely evident in the meteorogram. The leucocytes began to increase, the eosinophils reached a crest and so did the percentage of polymorphonuclear leucocytes. The whole organism was stimulated and while the blood pressure first increased on August 29, it then began to decline rather sharply. The respiratory rate first held its own but the pulse rate increased.

The examiner will now note the date of September 15. A line has been drawn vertically through the curve for this date, indicated by circles **(15)** both in the meteorogram and in the lower portion of the curve. This period was one with a sharp autumnal transition, with severe rains, with wide swings in environmental temperature, and associated with the first marked autumnal increase in barometric pressure.

Obviously this period of environmental strain was followed by marked evidence of fatigue on the part of the patient:

In the first place the leucocytes reached a crest on September 21, and the percentage of polymorphonuclear leucocytes increased, the while the eosinophils actually disappeared after this time.

On September 15, it will be observed that the methylene-blue time was reduced **(T)** and a respiratory crest occurred **(U)**; both respiratory rate and pulse rate increased progressively after this time.

A fever crest **(W)** was reached with wide swings in amplitude.

After the period the course of the patient was progressively downhill, with diastolic blood pressure gradually declining to low levels (fatigue), with body temperature declining, leucocytes declining after the early part of October, and clinical symptomatology increased.

Death followed with the passage of a polar front on November 17, 1936.

The Clinical Episodes

To illustrate the association of the subjective symptoms of the patient with the weather changes, the events recorded in the clinical history during October and November are graphed under nine episodes. These are as follows:

(1) October 6, 7 and 8: The patient first complained of being tired and of having had a poor night; abdomen tender.
(2) October 12: Chest pain; drowsy.
(3) October 16 and 17: Chest pain.
(4) October 19: Chest pain; slept poorly.

(5) October 21 to 24: Dyspnoea, cough worse, chest pain, hoarseness, sore throat.

(6) October 27 to 31: Poor night; chills, weakness, sore throat, chest pain, abdominal pain, cyanosis, dyspnoea.

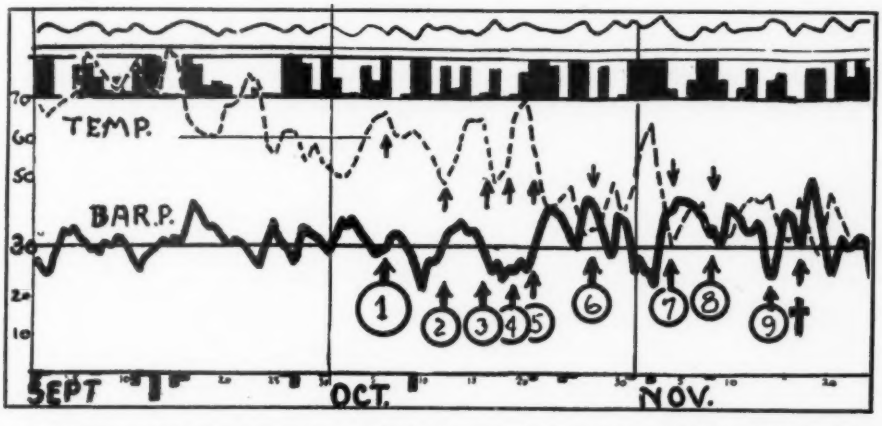
(7) November 4: Chest pain.

(8) November 8 and 9: Poor night; chilly, dyspnoea, cyanosis, weakness.

(9) November 14: Flushed, cyanotic.

(10) The final clinical episode, with dyspnoea, cyanosis, confusion on November 16, and death of the patient on November 17.

When we now relate these ten clinical episodes to the meteorological condition of the time as illustrated in text figure 3 it will be ob-



TEXT FIG. 3. Meteorogram to illustrate the association of ten clinical episodes with the meteorological situation of the time in tuberculosis subject 1. Clinical episodes numbered (1) to (9) with death of the patient on November 17.

served that episode (1) occurred with the passage of a polar front. Episode (2) occurred with the next increase in barometric pressure and when temperatures had temporarily reached a low.

Episode (3) occurred with a fall in temperature from a high and episode (4) with the beginning of an increase in barometric pressure with low temperatures.

Then followed episode (5) with the passage of a polar air mass, and with the crest of the barometric pressure we observe episode (6).

Episode (7) occurred with the next barometric episode early in November and episode (8) with the succeeding fall in temperature, while episode (9) is recorded at the time of a barometric low, and death finally occurred with the passage of the next barometric low.

The Postmortem Diagnosis[2]

White male, 169 cm. in length, 105 lbs. in weight.

1: Chronic fibrocaseous pulmonary tuberculosis with cavitation.

2: Fibrous obliteration of both pleural cavities.

3: Marked chronic passive congestion of the liver with atrophy and fatty degeneration.

4: Tuberculous ulcers of the terminal ileum.

5: Acute splenic tumor with miliary tubercles.

6: Chronic cholecystitis and cholelithiasis.

7: Thrombosis of the veins along the left lateral wall of the bladder and pelvis.

8: Ascites.

DISCUSSION

That the development of the clinical picture reflecting the progression of the tuberculous infection is conditioned not only by the inherent organic constitutional resistance but by environmental strain and therapeutic alkalinization, is clearly portrayed even in this relatively short period of observation of the patient.

Illness began in the winter (February, 1931) and a second episode followed five years later, when in the spring of 1936 the pH levels had reached the lowest point of the year. This is indicated in text figure 4 in which our pH data for all of our subjects have been graphed (6a).

Of interest in this connection is the fact that the years intervening from 1931 to 1936 had been years of less environmental strain than usual (phase of sun spot decline) while the late winter in 1936 was one of unusual cold and consequently of unusual demand on the energy stores.

When first examined in August, 1936, the second and final phase of activation had so far progressed that the patient had a high temperature, pulse rate and respiratory rate and the roentgenological examination revealed a far advanced stage.

We then could, by therapeutic intervention (sodium citrate), actively step up the sympathicotonic effectiveness on the blood pressure and induce a pressor crest, as was evident on November 2, but here this is of practically no value, indeed may be harmful because it merely throws a greater load on the myocardium and ultimately the fatigue finds

[2] To economize space the details of the postmortem protocols and the microscopic examination of the tissues are not included.

THE PROTOCOL OF LABORATORY OBSERVATIONS—SUBJECT 1

DATE, 1936	MONOCYTE-LYMPHOCYTE RATIO	POLYNUCLEARS	IMMATURE FORMS	LYMPHOCYTES	MONOCYTES	EOSINOPHILS	BASOPHILS	BLOOD PRESSURE	PULSE RATE	RESPIRATORY RATE	TEMPERATURE	METHYLENE BLUE DISAPPEARANCE TIME	TOTAL LEUCOCYTES	
Aug. 25	0	81	7	11	0	1	0	118/76	124	36	102.2–102.2	7	8,350	Weak Weight 119½ lbs.
26	0	86	2	11	0	1	0	124/84	120	30	102.0–102.8	9	9,750	Coughing
27	0	87	2	10	0	1	0	114/74	116	32	101.4–102.8	10	7,630	Better
28	0	90	1	9	0	0	0	120/70	116	32	101.6–102.2	11	10,850	Same
29	.25	92	3	4	1	0	0	128/78	124	34	100.0–102.8	7	9,100	Same
30	—	—	—	—	—	—	—	—	—	—	100.0–103.2	—	—	
31	0	93	3	4	0	0	0	110/70	112	32	101.0–103.0	—	9,600	Same Weight 121½ lbs.
Sept. 1	0	86	2	10	0	2	0	116/78	128	36	101.0–103.0		11,200	Fair
2	0	91	0	9	0	0	0	118/82	120	28	101.8–103.2	11	9,650	Fairly good
3	0	87	3	9	0	1	0	112/78	132	36	100.4–101.8	9	11,400	Same
4	0	88	1	11	0	0	0	116/70	136	32	101.2–102.6	9	—	Same
5	0	81	6	8	0	5	0	—	—	—	101.0–102.6	—	—	
6	—	—	—	—	—	—	—	—	—	—	100.4–103.6	—	—	
7	—	—	—	—	—	—	—	—	—	—	100.8–103.0	—	—	
8	—	—	—	—	—	—	—	118/78	120	28	101.4–102.6	10	13,550	Good Weight 117 lbs.
9	—	—	—	—	—	—	—	106/68	124	34	99.4–104.0	24	10,150	Good
10	0	85	6	8	0	1	0	118/78	116	30	100.0–103.0	24	12,600	Same
11	0	81	4	14	0	1	0	108/72	136	32	100.6–103.4	24	13,300	Same
12	0	87	2	11	0	0	0	102/62	128	36	100.2–103.4	24	14,100	Same
13	0	—	—	—	—	—	—	—	—	—	99.0–103.0	—	—	
14	0	86	3	11	0	0	0	108/72	120	36	100.6–102.8	24	10,750	Good
15	0	90	3	7	0	0	0	118/68	132	38	98.8–104.0	12	—	Good
16	0	86	5	9	0	0	0	100/70	120	32	101.6–102.0	24	13,500	Good
17	0	89	7	4	0	0	0	104/62	120	34	101.2–102.4	24	14,050	Good
18	0	90	3	6	0	1	0	110/74	124	36	100.6–101.0	20	15,700	Good
19	0	—	—	—	—	—	—	112/68	128	32	101.2–103.0	20	13,800	Good
20	0	—	—	—	—	—	—	—	—	—	101.6–102.8	—	—	
21	0	92	1	7	0	0	0	108/68	140	36	102.4–102.0	24	17,300	Same Weight 112½ lbs.
22	0	93	3	4	0	0	0	106/72	140	40	99.8–103.6	24	15,500	Same
23	0	82	2	16	0	0	0	98/58	140	44	100.6–101.2	12	12,700	Always says he feels all right but doesn't seem as well
24	0	90	3	7	0	0	0	106/68	136	36	101.6–103.0	20	13,450	Drowsy
25	.07	81	4	14	1	0	0	114/74	128	36	100.8–102.4	12	11,900	Same
26	.3	85	1	11	3	0	0	110/70	124	40	103.0–103.8	—	12,050	Same
27	—	—	—	—	—	—	—	—	—	—	102.4–103.8	—	—	
28	0	91	0	9	0	0	0	108/70	132	44	102.4–103.0	24	13,250	Says toes are usually numb
29	0	93	1	6	0	0	0	108/72	128	38	101.6–101.0	12	10,000	Good
30	.14	79	5	14	2	0	0	108/68	128	44	99.4–103.0	24	14,250	Fairly good; feels chilly
Oct. 1	0	90	3	7	0	0	0	106/70	136	38	101.0–102.4	12	13,000	Fairly good
2	0	91	3	6	0	0	0	98/66	136	36	101.4–101.2	24	13,550	Fairly good
3	.2	90	4	5	1	0	0	102/74	124	40	101.0–101.8	—	16,850	Same
4	—	—	—	—	—	—	—	—	—	—	102.2–102.2	—	—	
5	0	90	4	6	0	0	0	104/70	132	36	100.6–102.6	12	13,350	Can't understand why worried about his weight Weight 103 lbs.
6	0	93	2	5	0	0	0	108/70	128	36	101.4–103.0	24	14,800	Fair
7	.1	86	3	10	1	0	0	106/70	128	36	98.9–102.4	12	—	Weaker

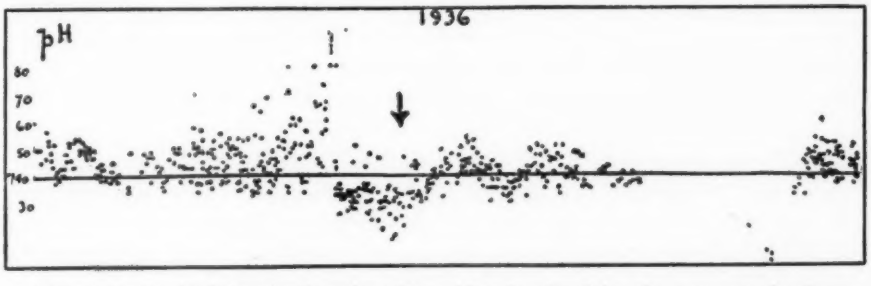
THE PROTOCOL OF LABORATORY OBSERVATIONS—SUBJECT 1—*Concluded*

DATE, 1936	MONOCYTE-LYMPHOCYTE RATIO	POLYNUCLEARS	IMMATURE FORMS	LYMPHOCYTES	MONOCYTES	EOSINOPHILS	BASOPHILS	BLOOD PRESSURE	PULSE RATE	RESPIRATORY RATE	TEMPERATURE	METHYLENE BLUE DISAPPEARANCE TIME	TOTAL LEUCOCYTES	
Oct. 8	0	91	4	5	0	0	0	106/70	124	30	100.4–102.0	24	11,000	Fair
9	0	91	3	6	0	0	0	116/74	120	36	101.0–102.0	20	13,850	Fair
10	0	84	8	8	0	0	0	104/68	124	40	101.0–102.0	12	22,250	Fair
11	—	—	—	—	—	—	—	—	—	—	101.4–101.8	—	—	
12	0	86	6	8	0	0	0	112/68	128	34	99.6–102.2	24	18,600	Fair
13	0	90	2	7	0	1	0	106/62	120	36	100.4–102.6	24	15,450	As usual
14	.1	85	4	10	1	0	0	108/70	134	36	102.4–102.6	48	17,450	Does not feel well; aches all over, especially legs
15	0	90	2	8	0	0	0	112/74	120	32	98.6–101.6	36	15,900	About same
16	0	90	2	8	0	0	0	106/64	128	44	99.6–102.0	12	12,550	About same
17	0	89	3	8	0	0	0	104/64	120	38	99.0–101.2	12	14,400	Sleepy
18	—	—	—	—	—	—	—	—	—	—	99.0–102.2	—	—	
19	0	87	4	9	0	0	0	106/68	128	36	99.0–103.0	96	18,500	Feels fine but sleepy
20	0	92	4	4	0	0	0	106/70	120	40	99.0–101.4	96	14,800	Drowsy
21	0	93	0	7	0	0	0	96/58	124	36	98.6–102.0	72	14,450	Tired, stiff and aches all over
22	0	92	3	5	0	0	0	100/64	124	32	100.0–102.0	72	13,950	Looks better
23	—	—	—	—	—	—	—	108/70	120	32	101.2–102.0	48	18,650	Fair
24	—	—	—	—	—	—	—	102/62	132	40	101.0–103.0	12	12,700	About the same
25	—	—	—	—	—	—	—	—	—	—	99.2–103.8	—	—	
26	.67	94	1	3	2	0	0	102/50	132	36	101.6–101.4	38	11,250	Stiff all over
27	0	90	1	9	0	0	0	106/76	120	34	99.4–100.2	24	17,800	Not so well; says everything is wrong
28	0	93	2	5	0	0	0	106/68	118	32	100.6–102.0	36	13,550	Sleepy
29	.17	87	6	6	1	0	0	112/74	124	38	101.0–102.0	30	12,750	Fair; started sodium citrate 5.0 g. daily
30	.28	87	4	7	2	0	0	108/68	120	36	98.6– 99.8	10	14,000	Fair
31	0	91	3	6	0	0	0	112/78	132	40	97.6–101.6	20	12,200	Sleepy
Nov. 1	—	—	—	—	—	—	—	—	—	—	102.0–100.6	—	—	
2	.25	93	2	4	1	0	0	136/70	120	36	101.0–102.4	24	13,400	A little better; coughing
3	—	89	3	8	0	0	0	122/78	124	36	101.0–102.0	—	10,300	Same
4	—	—	—	—	—	—	—	—	—	—	100.8–102.6	—	—	
5	—	—	—	—	—	—	—	112/70	120	34	98.0–101.0	—	—	Coughing; feels all right
6	0	88	6	6	0	0	0	106/74	100	30	98.6–101.6	—	11,200	Good
7	.4	89	4	5	2	0	0	112/68	130	40	99.6–101.0	—	11,700	Coughing; feels same
8	—	—	—	—	—	—	—	—	—	—	97.0–102.0	—	—	
9	—	—	—	—	—	—	—	96/50	—	—	99.4–100.4	—	11,700	Feels much worse
10	0	93	4	3	0	0	0	104/64	120	28	98.6–102.8	34	9,100	Feels and looks much better; no coughing
11	0	92	2	6	0	0	0	116/74	116	30	98.0–102.6	12	10,450	Feels all right
12	0	90	4	6	0	0	0	116/78	120	34	97.8– 99.6	24	12,950	Fine
13	0	95	1	4	0	0	0	108/68	120	36	99.6–101.0	24	10,400	Fair
14	0	90	5	5	0	0	0	112/78	124	28	98.6–101.6	—	15,500	Fair
15	—	—	—	—	—	—	—	—	—		101.2–101.8	—	—	
16	0	88	5	7	0	0	0	116/78	128	36	97.8–100.4	—	7,650	Says he feels fair; appears drowsy; face slightly puffed, high color
17	.14	92	0	7	1	0	0	—	120	36	99.0– —	—	10,350	Sleeping on side; labored breathing Expired 2:45 p.m.

expression in the diastolic low of November 9. This decline is materially enhanced by the effect of the cold air mass which began to pass on the 3rd of the month.

Of particular interest, too, is the skin reaction-time for the disappearance of intracutaneously injected methylene-blue, which in this patient revealed wide fluctuations from day to day. Casual inspection of the graph will immediately make evident that periods of increased respiratory activity are associated with periods when the methylene-blue disappearance time is shortened, that is, when we presumably deal with relative air hunger of the tissues (curve (7) on the biometeorogram).

Attention is finally directed to the disappearance of the eosinophils from the blood picture shortly after the admission of the patient, and finally to the fact that each change in the symptomatic picture was in



TEXT FIG. 4. pH determinations for 1936. Note low level for the group at the down-turned arrow (period of activation in tuberculosis subject 1).

turn related to an environmental alteration. As the individual became sicker, environmental susceptibility was magnified.

TUBERCULOSIS SUBJECT 2—ADVANCED CASE—IMPROVEMENT UNDER OBSERVATION

In the next case we deal with a tuberculous process involving the right upper lobe which had been active for at least three years. The clinical record of the Research and Educational Hospital follows:

Clinical History

H. G., a white male, thirty-eight years of age, was well until October, 1933, when he had an attack of pleurisy in his left chest. He was confined to bed at home under the care of a physician for two months, during which time he lost 35 pounds in weight. He made a fairly good recovery and returned to work as a barber. For the following three years he was well except for easy fatigability.

In the last week of September, 1936 (1) (text figure 5), he contracted a "chest cold" and awoke with a sharp pain in his right chest, worse on cough or inspiration. At the same time he first noticed a productive cough and on several occasions subsequently had blood-streaked sputum. These symptoms continued while he remained in bed at home for one week, and he was admitted to the Cook County Hospital on October 1, 1936 (2) (text figure 5). Here, chest X-ray films and sputum examinations were done. After eight weeks of treatment as an ambulatory patient he was transferred to the Research and Educational Hospital.

In the past history he had measles, mumps and scarlet fever as a child. The family history was apparently negative and there was no record of tuberculosis in the family. He drank one-half pint of liquor daily for the past year and smoked three to four cigarettes daily.

Physical examination revealed a well developed but thin white male of thirty-eight who did not appear acutely ill. The head, eyes, ears and nose were essentially normal. Teeth were carious and pharynx was slightly injected. Chest was symmetrical and moved normally. Over the right apex was a slightly diminished resonance on percussion with moist posttussive râles in the same area. The heart borders were within normal limits and the sounds were of good quality with no murmurs present. Pulses were regular and equal. Abdomen revealed no masses or tenderness. Genitalia were those of a normal male. The extremities were normal and symmetrical except for moderate clubbing of the fingers. Clinical impression was that of tuberculosis of the right pulmonary apex.

The Kahn test was negative and the urine was normal. Serum albumin was 3.74 per cent, serum globulin 3.6 per cent; haemoglobin 11.0 g., red blood corpuscles 5,200,000; white blood cells 12,500.

Roentgenological examination made on December 5, 1936 (roentgenogram 3) showed irregular increased density over the right apex and first and second interspaces suggestive of tuberculous infiltration.

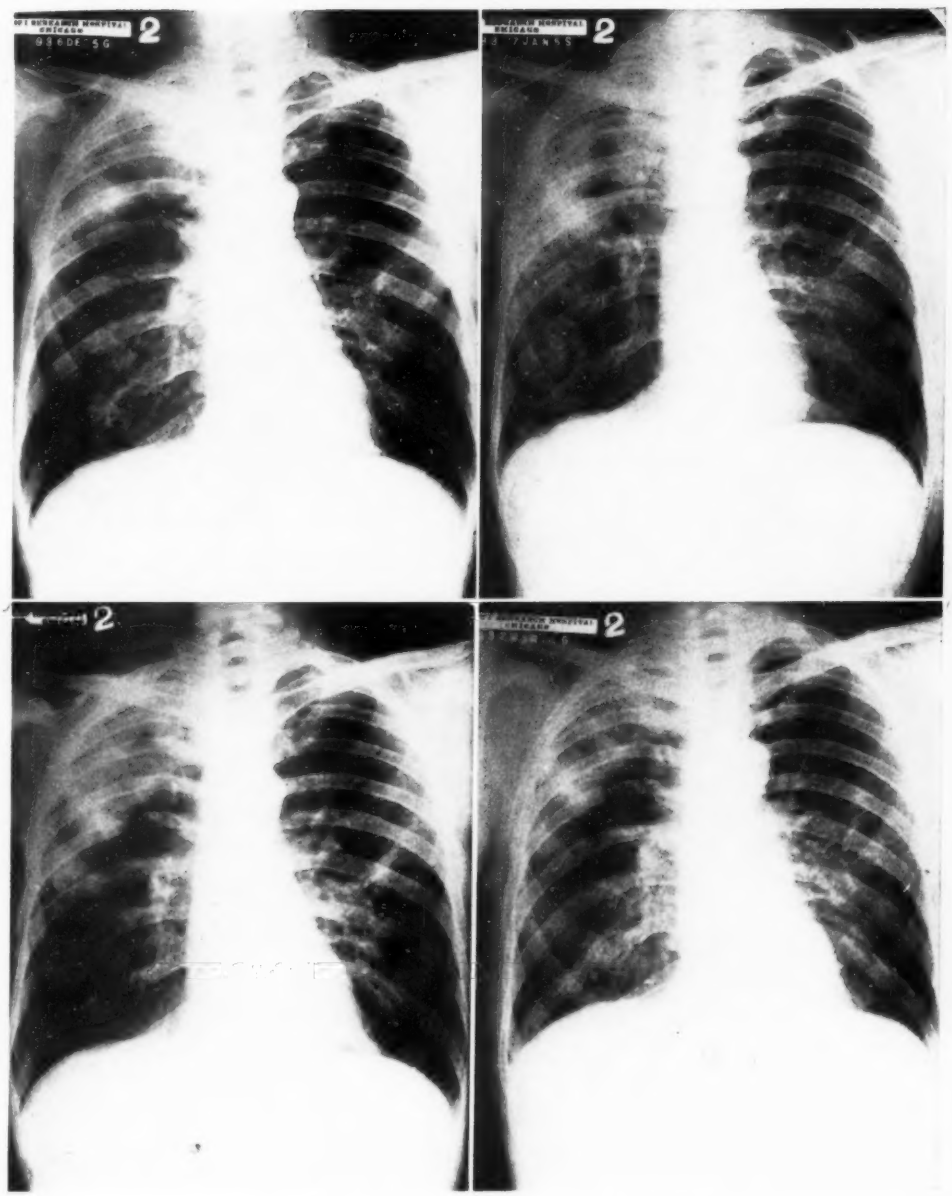
Examination made January 4, 1937 (roentgenogram 4) showed extension of process noted on previous examination, densities extending considerably farther down into the right lung. Some localized radiolucent areas were present suggestive of cavity formation.

Examination made February 9, 1937 (roentgenogram 5) showed practically the same findings noted on previous examination.

Examination made March 11, 1937 (roentgenogram 6) showed some regressive changes.

The Weather at the Onset

The onset record is of interest insofar as it occurred in the autumn of 1933 and later reactivation again became evident in the autumn, this time three years later.



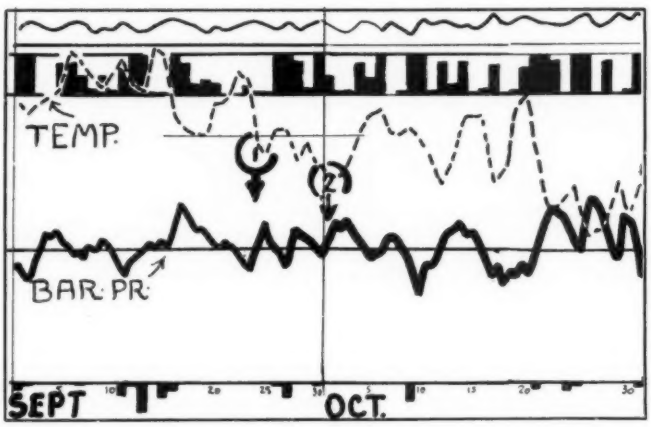
ROENTGENOGRAM 3. (upper left) December 5, 1936
ROENTGENOGRAM 4. (upper right) January 4, 1937
ROENTGENOGRAM 5. (lower left) February 9, 1937
ROENTGENOGRAM 6. (lower right) March 11, 1937

A meteorogram (text figure 5) of the time illustrates the fact that this second activation was associated with a sharp change from the high temperature of September to autumnal lows **(1)**. At this time there was marked precipitation, most evident on September 27. Admission to the hospital followed **(2)** with the barometric crest in the graph and with the lowest temperatures of the time.

The patient was observed from the end of November, 1936 to April, 1937.

The Biometeorogram

The graph (text figure 6) has a meteorogram superimposed **(1)**. Then follow curves of the leucocytes, including the differentials, the eosinophils **(5)**,



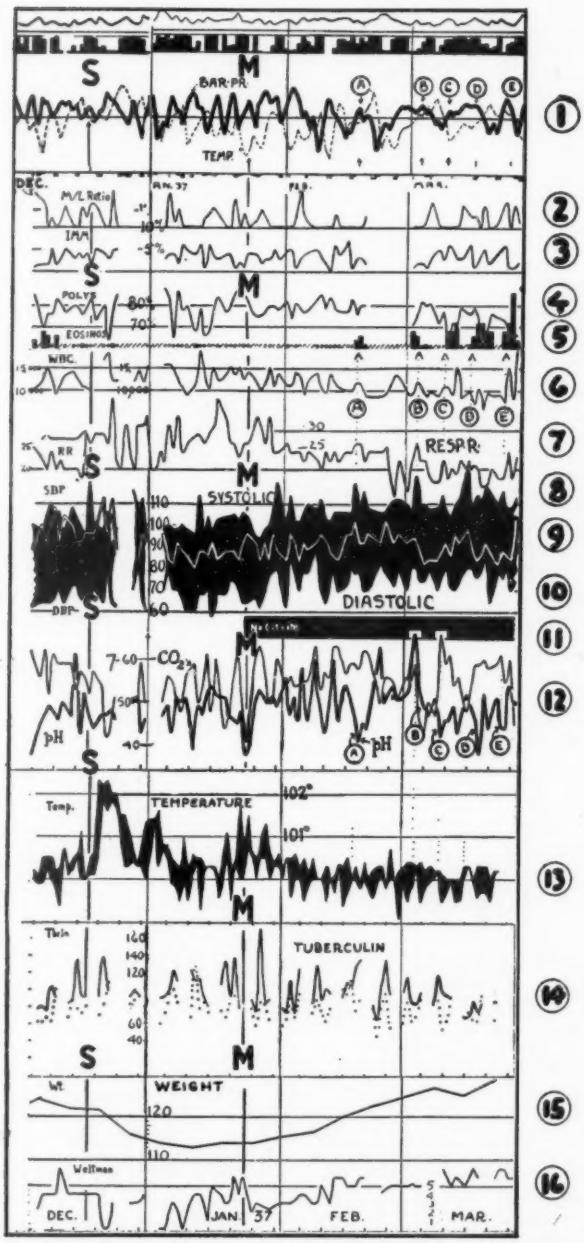
TEXT FIG. 5. Meteorogram to illustrate the clinical events in tuberculosis subject 2

polymorphonuclear leucocytes **(4)**, the percentage of immature forms **(3)** and the monocyte-leucocyte ratio **(2)**.

Next the curve of the respiratory rate **(7)** and the blood pressure **(8)** to **(10)** with the pulse rate carried as a white curve in the black field **(9)**, CO_2 content **(11)** and the blood pH **(12)**, the patient's temperature **(13)** (maximal and minimal of the day), quantitative tuberculin reaction **(14)**, the weight **(15)**, the Weltmann reaction **(16)**.

Sodium citrate was administered from January 23 to the close of the period of observation (black bar at **(11)**).

We have here been interested to observe the unfavorable effect of the inclement season (weather) and to note whether alkalinization would have any effect in counteracting this situation.



TEXT FIG. 6. Biometeorogram of tuberculosis subject 2. See text for detailed description

Vertical line **(S)** subjective activation
Vertical line **(M)** alkalinization commenced
Eosinophilic crests **(A)**, **(B)**, **(C)**, **(D)** and **(E)**

Clinical Notes

1936		
Dec.	6	Cough
	7	Dyspnoea
	8	Chest pain and cold
	9	Tired
	10	Tired and cough
	11	Cough
	12	Tired
	13	
	14	Cough
	15	Tired, night sweats
	16	
	17	Cough, chest pain, haemoptysis
(S)	18	Cough, chest pain, tired
	19	Tired
	20	Nausea, chill, fever, night sweats
	21	Emesis, chills, fever, night sweats
	22	Emesis, chest pain, dyspnoea
	23	Emesis
	24	
	25	Cold and tired
	26	Cold
	27	Cold
	28	Tired, anorexia
	29	
	30	
	31	Tired
1937		
Jan.	1	
	2	Anorexia
	3	Anorexia
	4	Nausea
	5	Cough, dyspnoea, tired
1937		
Jan.	12	Cough
	22	Pain in the hips
(M)	23	Appetite poor
	24	Appetite poor
	25	Appetite poor
	26	Abdominal cramps
	27	Abdominal cramps
	28	
	29	Cough worse
	30	
	31	
Feb.	2	Cough worse
	5	Cough worse
	10	Cough worse
	11	Joint pain and stiffness
(A)	18	Sore throat
	19	Sore throat
	20	Sore throat
	22	Head cold
	23	Head cold
	25	Head cold
	25	Head cold and headache
	26	Head cold
	27	Joint pain and right shoulder sore
Mar.	1	Cough worse
(B)	2	Tired
(C)	10	Cough
	13	Joints are stiff
	21	Pain in the right shoulder
	22	Pain in the right shoulder
	23	Pain in the right shoulder
	25	Intoxicated
	26	Released

Activation was observed clinically during December at which time the patient had night sweats, chest pain and haemoptysis on the 17th, that is, with a polar episode.

On the 18th of the month we have extended a vertical line through the graph, marked **(S)** (symptoms) to facilitate study of the changes.

It will be observed that a sharp pressor crest **(8)** occurred and at the same time the diastolic pressure was low **(10)**, throwing greater cardiac strain on the vascular system.

A febrile crest followed with its crest two days later **(13)**.

Coincident with this the pH sinks **(12)**.

Leucocytes increase to a crest of 18,000 on the 22nd **(6)**.

The eosinophils apparently disappear **(5)**.

The pulse rate increased markedly **(9)**.

The weight declined at the time **(15)** and the Weltmann reaction is diminished **(16)**.

Another blood pressure crest occurred with the passage of polar air masses at the end of December. There was marked precipitation at this time and a sharp barometric crest evident on the 28th. A blood pressure crest was observed on the 28th; and pH again was lower on the 30th and a febrile reaction followed. The patient felt badly.

Following this, several polar air masses, characterized by their sharp barometric crests, passed and by the 14th the patient again revealed an increase in the respiratory rate. This was followed by a febrile increase on the 17th, at which time the patient again began to complain of pain in the chest.

At this time alkalinization was commenced indicated by the circle **(M)** and black bar on the graph.

This was followed:

1: By a decline in temperature.
2: By an increase in blood pressure.
3: By an increase in weight.
4: By an increase in the Weltmann reaction.
5: By a reduction in the respiratory rate and in the leucocyte count.
6: By a tendency of the blood pH to increase.

Of particular interest is the return of the eosinophils as the patient improved.

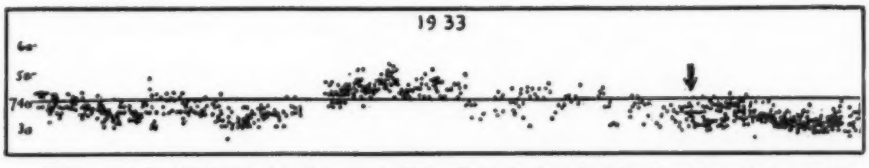
Eosinophilic crests as criteria of improvement: As we study the curve, it will be observed, that five distinct periods of eosinophilic increase were to be observed, these have been lettered **(A), (B), (C), (D)** and **(E).** They correspond to coincident increases in the systolic blood pressure and in turn with the passage of polar air masses (note barometric crests). In other words, we are here dealing with a period of relative anoxia, associated with an increase not only in systolic blood pressure, but this was followed in turn by an increase in respiratory rate as well as by CO_2 content in the blood, but now the efficiency of the bone marrow was indicated by the production of eosinophilic cells. What is perhaps of more clinical importance, was the observation that now no febrile increases follow such periods of stimulation. On the contrary, the patient was apparently definitely improved after each period of stimulation.

The patient was finally discharged because of insubordination.

DISCUSSION

In this case the first evidence of activity in October, 1933 also occurred at a time when the pH levels of our test population were relatively low, as indicated by text figure 7 on which our daily titrations for the control group are indicated by dots.

The immediate activation in the last week of September, 1936 permits us to refer to the case just studied to observe the presumptive biological status of the patient and we can note from text figure 2 that at that time the respiratory rate in tuberculosis subject 1 had reached a crest, leucocytes increased rapidly after the 29th of the month, pulse rate reached a crest on the 1st and 2nd of October. In other words, we then had evidence that the period of environmental temperature decline, with marked precipitation at the cyclonic interface on the 26th and 27th of September, resulted in a considerable organic disturbance in the patient then under observation.



TEXT FIG. 7. pH levels for the year 1933. Period of activation in tuberculosis subject 2 indicated by arrow.

In this patient the comprehensive biometeorogram (text figure 6) presents a totally different picture from that in tuberculosis subject 1. Despite the fact that that season was inclement the patient began to improve rapidly with the institution of an alkalin regimen. It is to be noted that the weight increased, temperature declined, pH levels remained high, the respiratory rate declined, as did the leucocytes.

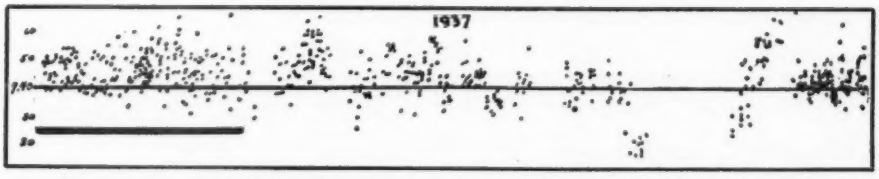
Whether or not this was spontaneous and due to inherent resistance of the subject, or whether it was due incidentally to a generally higher level of the acid-base balance indicated for our control group and to be observed in text figure 8, is problematical.

In the comprehensive biometeorogram two periods of increased activity have been indicated by the vertical stippled lines marked **(S)** and **(M)** and the characteristic effects on the various reactions have been discussed; both these periods were associated with clinical effects as well as marked vascular and chemical reactions and with the period **(M)** the lowest pH level of the time was recorded.

Because of the observation that the appearance of eosinophils in the blood stream heralds a rather favorable bone marrow reaction (6b), five such episodes were lettered **(A), (B), (C), (D)** and **(E)** and followed in the latter part of the period of study.

One gains the impression that the subject was made resistant to the meteorological effects and their physiological consequence and, instead of being harmed by the passage of cold air masses, the patient was actually improved by each episode. Inasmuch as this change in the clinical picture occurred during a period of the year when the normal trend is unfavorable, the possibility must be considered that this improvement was associated with alkalinization.

Of importance is the recognition of the seeming paradox of weather effects—that the passage of a cold air mass may in one instance cause stimulation followed by fatigue as the outstanding clinical effect, on the other hand, stimulation associated with clinical improvement.



TEXT FIG. 8. pH levels for the year 1937. Period of study in tuberculosis subject 2 indicated by black bar.

TUBERCULOSIS SUBJECT 3—FAR ADVANCED CASE—FATAL TERMINATION

We turn again to a case that terminated fatally after a nine months' period of observation.

It concerned a white male, fifty-one years of age, who had apparently revealed evidence of some clinical activation for a period of ten years before the time of study. The patient expired on August 10, 1936.

Clinical History

F. S., a fifty-one year old single white male of Mexican descent, was in fairly good health until about Christmas time of 1933 **(1)**. For ten years he had one or more severe colds every winter, lasting about ten days and followed by recovery. In December, 1933 he had one of these colds which persisted throughout the winter with purulent nasal discharge and productive cough.

In May, 1934 (about May 12) **(2)** he developed fever, pain in the right chest anteriorly, worse on deep breathing or coughing, and was admitted to Cook County Hospital where he was told he had pneumonia.

He was discharged after three weeks, still feeling very weak, and was treated at home for a period of four months, during which his cough and pain in the chest persisted. He became progressively weaker and continued to lose weight. On October 8, 1934 **(3)** he returned to Cook County Hospital where he was told he had tuberculosis and was admitted to the Tuberculosis Hospital on October 17, 1934.

After six months he was allowed a short walk around the ward. About July, 1935 (last of month) he began running a fever up to 102° to 103° F. and was put back to bed for a month, after which he was allowed bathroom privileges and felt well.

At 11 p.m. on September 17, 1935 **(4)** the patient awoke with a coughing spell and had a haemoptysis filling three emesis basins with dark blood. At 7 a.m. on September 18 haemoptysis had about ceased and he had none thereafter. He was kept strictly in bed. He felt very weak for about twenty-five days and was then allowed bathroom privileges again. At the time of admission to the Research and Educational Hospital he felt fairly well except for a persistent and productive cough which had improved somewhat since September.

His past history revealed that he had rheumatism of the legs when seven and an attack of "catarrhal jaundice" characterized by nausea and vomiting, jaundice of the skin and sclerae but no abdominal pain. He recovered in five weeks. He had no colds or sore throats until ten years ago.

History of the cardio-respiratory, gastrointestinal and neuromuscular systems was normal. Genitourinary history was normal except for gonorrhoea about thirty years ago, and treatment for "bad blood" with 9 intravenous and intramuscular injections in April and May, 1934.

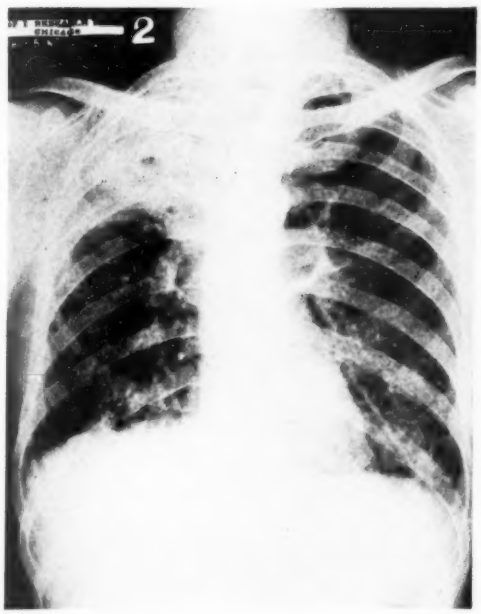
He was born in Mazatlan, Sivaloa, and came to Washington in 1908. He roamed the country as a round-house man and day laborer. He smoked a pack of cigarettes daily until a year ago and drank an occasional glass of beer or whiskey one or two times a week. The family history was vague, but there was no record of tuberculosis.

Physical examination revealed an underdeveloped and moderately emaciated Mexican male of about forty-seven years, lying quietly in bed in no apparent distress. There was no sinus or mastoid tenderness. The pupils were circular and equal and reacted to light and accommodation. The mucous membrane of the mouth was slightly injected and the teeth were in fair condition. The posterior cervical lymph nodes of the neck were palpable; the thyroid gland was not felt. The chest was the flat type with prominent ribs. Over the right posterior chest there was impairment of percussion note, increased tractile fremitus and increased transmission of spoken and whispered voice sounds and posttussive râles. In the right supraclavicular region the percussion note was hyperresonant, breathing was amphoric, and whispered

pectoriloquy and posttussive râles were present. The left chest showed no grossly abnormal physical signs.

The liver was just palpable at the costal margin. Kidneys and spleen were not felt. A large right indirect inguinal hernia was present, easily reducible. The heart was not enlarged to percussion, the sounds were weak and distant, but there were no murmurs. The testes were normal; there were numerous old scars and loss of pigmentation on glans penis and prepuce.

The skin was dry and rather loose, the extremities were symmetrical and thin, and the reflexes were normal and equal bilaterally. The impression was that



ROENTGENOGRAM 7. November 12, 1935

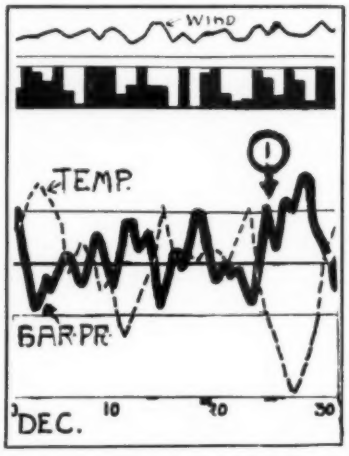
of pulmonary tuberculosis, with cavity at the right apex and infiltration of the right upper and lower lobes and an indirect inguinal hernia on the right side.

Roentgenological examination made November 12, 1935 (roentgenogram 7) showed increased density over the right apex, first interspace and part of the second interspace; a localized radiolucent area was present within the density. The tracheal shadow was displaced towards the right. These findings were consistent with an old tuberculous process with fibrosis and cavitation. There was also considerable increase of the linear markings extending into the lower lobes, especially on the right, suggestive of bronchiectasis. The right diaphragm showed evidences of pleuritic adhesions.

The Weather at the Onset

First episode: When we examine the meteorogram (text figure 9) of the dates associated with the onset of the disease, we note that the onset of clinical activity at Christmas, 1933 **(1)** occurred at a time when a severe cold wave passed over the region.

Inasmuch as the effect of this meteorological alteration has been carefully studied in the reactions of other individuals (8), we can definitely state that when this patient had his activation marked vascular spasm existed, which in turn was associated with anoxia and the production of capillary active substances. Under such conditions the resistance to the dissemination of bacteria would have been lessened.



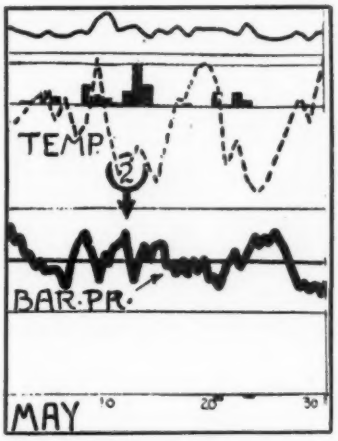
TEXT FIG. 9. Meteorogram to illustrate episode **(1)** in tuberculosis subject 3

Second episode: He developed fever, pain in the right chest, etc. about May 12, 1934 **(2)** (text figure 10). The period was one when high temperatures had prevailed on the 9th of the month, with the passage of a sharp cyclonic interface, high winds, low barometric pressure. This was followed (arrow) by a sharp fall in temperature and a barometric crest on the 12th of the month.

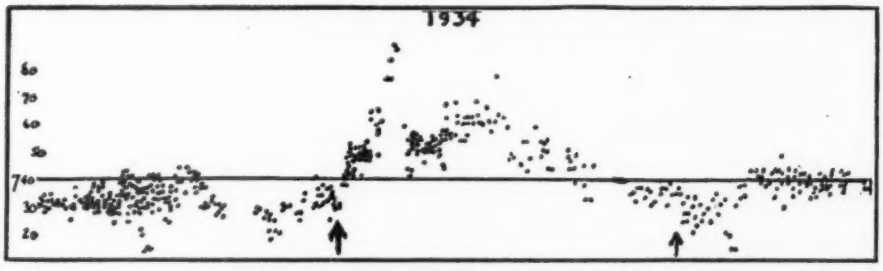
The significance of dating does not become apparent unless we can determine the probable biochemical conditions that existed in our patient at the time. We therefore first turn to the general pH curve of our control group (text figure 11) and note (first arrow) that this period was one when the pH levels were still low.

Then we turn to the record of a migraine patient examined at the

Research and Educational Hospital from early April to the end of May, 1934 for the day by day detailed changes. In the biometeorogram of this patient (text figure 12) the date of May 12 has been indicated by the circled arrow. This record actually reveals that this clinical episode in our tuberculous patient merely reflected activation due to lessened tissue resistance when the physiological status had been pushed toward



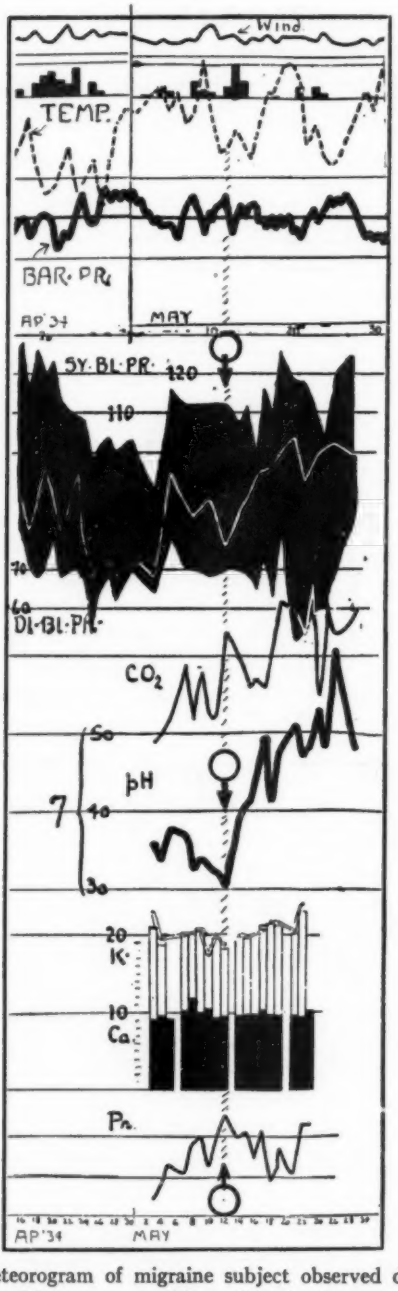
TEXT FIG. 10. Meteorogram to illustrate episode (2) in tuberculosis subject 3. Control observation.



TEXT FIG. 11. pH levels for control group for 1934. Arrows indicate activation in May and October, 1934, in tuberculosis subject 3.

the fatigue state by wide swings in environmental temperature; the actual low in the blood pH (7.30) was reached on the 12th of the month (text figure 12).

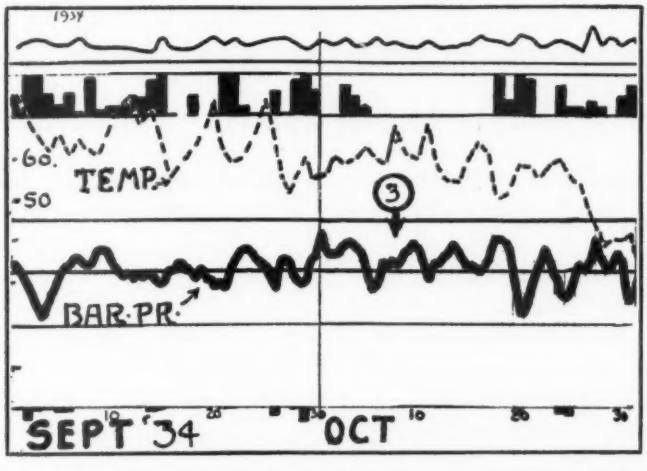
Third episode: The next episode, readmission to the Cook County Hospital on October 8, 1934, occurred at a time which has been discussed in considerable detail elsewhere. At the time (October 8) our control



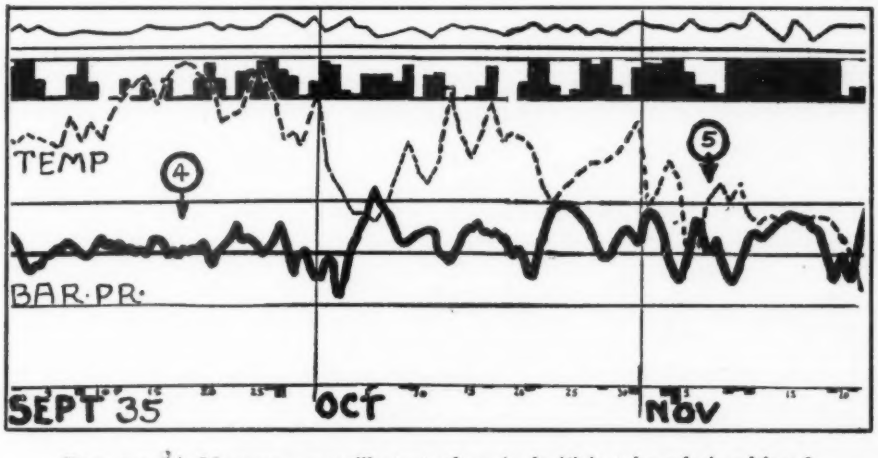
TEXT FIG. 12. Biometeorogram of migraine subject observed during April and May, 1934. (1) Upper curves—Meteorogram. (2) to (4) Blood pressure field. (3) Pulse rate. (5) CO_2 content. (6) Blood pH. (7) Potassium. (8) Calcium. (9) Blood protein. Circled arrows indicate date of May 12, 1934. Observe low pH at critical date.

subject revealed a major increase in the acid output of the urine, together with a retinal thrombosis (9).

Fourth episode: Severe haemoptysis was next recorded as of September 17, 1935 (4). From the meteorogram (text figure 14) it will be noted



TEXT FIG. 13. Meteorogram to illustrate episode (3) in tuberculosis subject 3



TEXT FIG. 14. Meteorogram to illustrate the episode (4) in tuberculosis subject 3

that this occurred with high environmental temperatures. The blood pressure as observed in other subjects on September 17 was unusually low (10), corresponding to a COD phase, when tissue digestion would

have been accentuated. Admission to the Research Hospital followed on November 7 **(5)**.

The Biometeorogram

In this patient we follow the course of events for the nine months preceding death and interrelate the meteorological environment with the biochemical reactions that occurred and in turn with the clinical phenomena that were associated.

The series of curves include (text figure 15):

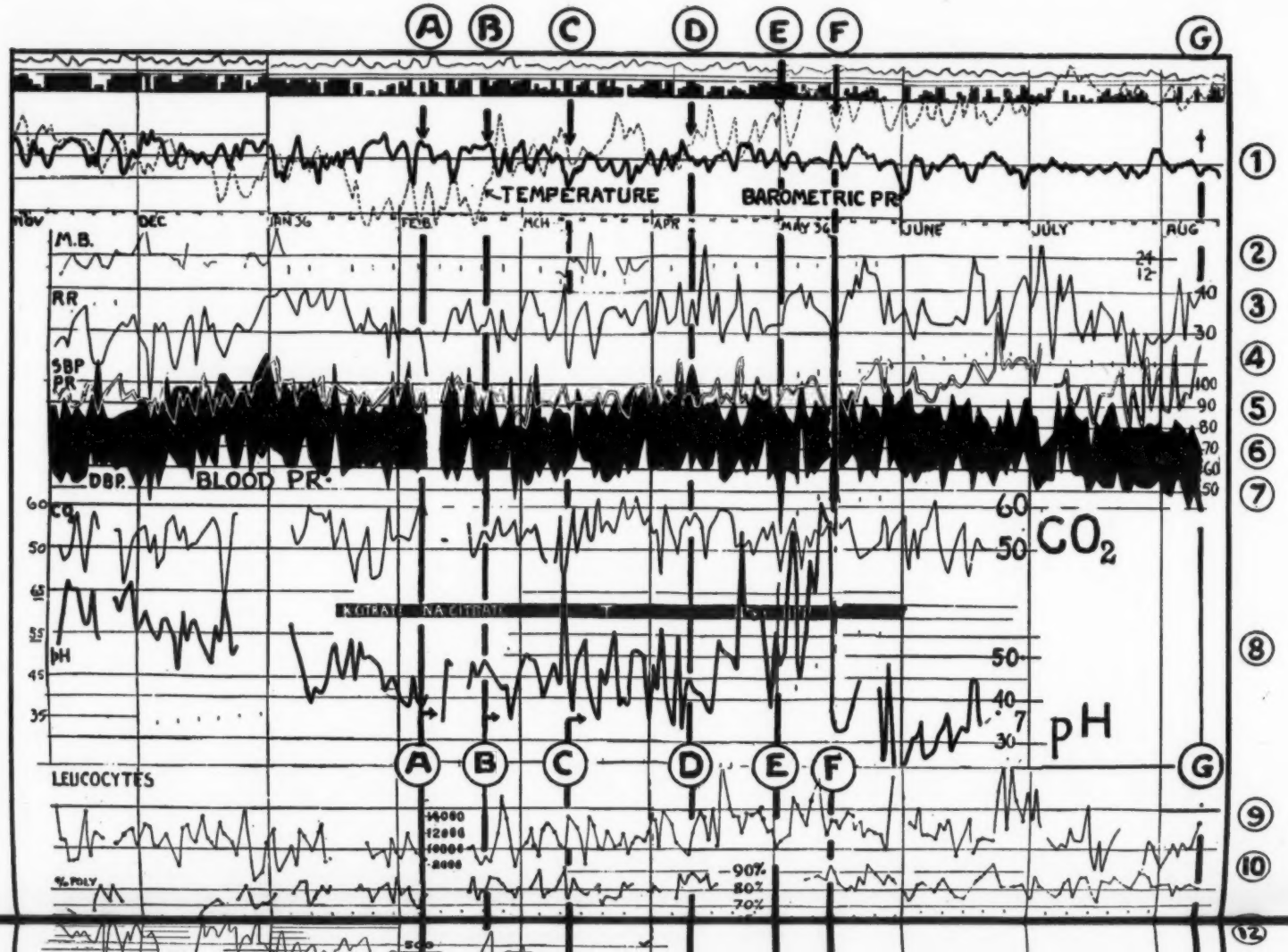
(1) Meteorogram, in which the top curve indicates wind velocity, then follow cloudiness, daily mean temperature (dotted line), barometric pressure (heavy line).
(2) M. B.—Methylene-blue disappearance time
(3) Respiratory rate
(4) Pulse rate (white line)
(5) Systolic blood pressure
(6) Diastolic blood pressure
(7) CO_2 content of venous blood
(8) Blood pH
(9) Leucocyte count
(10) Percentage of polymorphonuclear leucocytes
(11) Percentage of eosinophils
(12) Urinary volume
(13) Albumin (indicated for part of November and December, 1935)
(14) Daily maximal and minimal temperature
(15) Blood cholesterol
(16) Quantitative tuberculin reaction
(17) Electrical tissue resistance
(18) Weltmann reaction
(19) Sputum volume
(20) Gaffky count (for part of November)
(21) Weekly weight

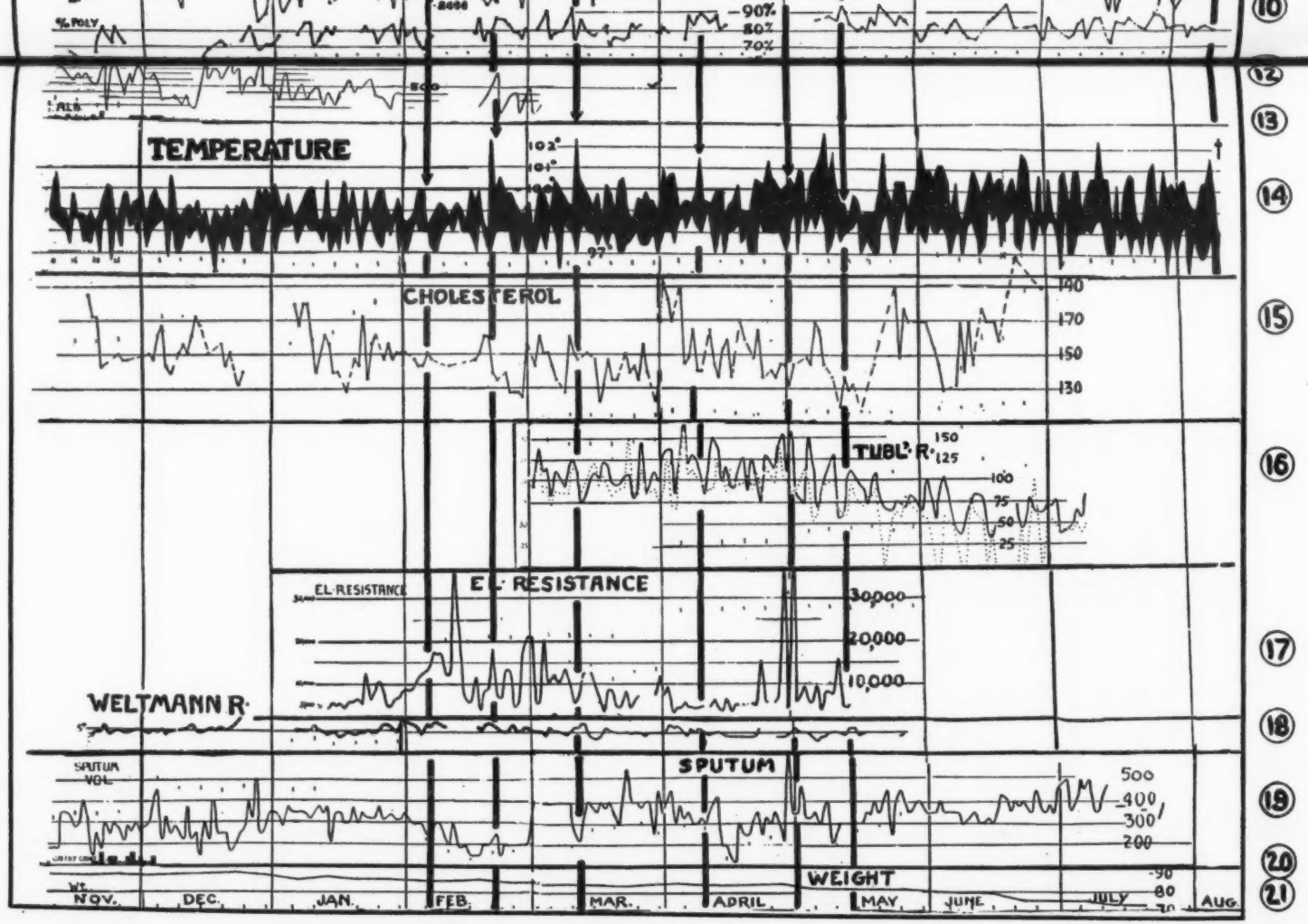
Clinical Notes

1935	
Nov. 12	Slept poorly
13	Cough, weakness
18	Cough, weakness
19	Pruritus
20	
21	Pruritus
22	
23	Dyspnoea
1935	
Nov. 24	Severe cough
Dec. 3	Tired, cough worse
13	Cough, weakness
14	Cough, weakness
30	Chest pain, cough
1936	
Jan. 16	Cough worse
Feb. 3	Tired
4	Tired

1936		
Feb.	5	
(A)	6	Chest pain, dyspnoea
	10	Pain, dyspnoea, sore throat
	11	Dyspnoea
	16	Tired, vomited
	17	
	18	Abdominal pain, vomited
(B)	21	Dyspnoea, chill, chest pain
	22	
	23	Dyspnoea
	25	Chest pain intermittent
	26	Chest pain
	27	Chest pain
	28	Dyspnoea
Mar.	1	Chest pain
	2	
	3	Chest pain
	4	Chest pain
	9	Chest pain, palpitation
	10	
	11	Chest pain, pruritus
(C)	12	Abdominal pain, vomited
	17	Nausea, vomited
	18	Abdominal pain, dyspnoea
	19	
	20	Dyspnoea
	21	Dyspnoea
	25	Choking spell
	28	Chest pain, severe dyspnoea
Apr.	2	Pain in precordium
	3	Chest pain, dyspnoea
	4	Chest pain, dyspnoea
	5	
	6	Dyspnoea
	7	Dyspnoea
	8	Dyspnoea
	9	Chest pain
(D)	10	Chest pain
	11	
	12	Dyspnoea, severe cough
	13	Feels better
	14	Feels better
	15	Feels better
	16	Nausea
	21	Chest pain
	22	Chest pain, dyspnoea
	23	
	24	Chest pain, dyspnoea
	27	Dyspnoea, severe cough
	28	Severe dyspnoea, chest pain
(E)	29	Severe dyspnoea, chest pain
	30	Severe dyspnoea, chest pain

1936		
May	4	Chest pain, dyspnoea, orthopnoea
	5	
	6	Dyspnoea, chest pain
	7	Dyspnoea
	8	Abdominal pain
	11	Chest pain, severe dyspnoea
	12	Chest pain
	13	Chest pain, vomited
(F)	14	Vomited
	15	Chest pain
	16	Chest pain
	17	
	18	Abdominal pain
	19	Abdominal pain, dyspnoea
	20	Dyspnoea, abdominal pain
	21	
	22	Chest pain
	23	Vomited
	24	
	25	Chest pain
	28	Chest pain, dyspnoea
	29	Chest pain
June	3	Chest pain, tired
	4	Chest pain
	5	Sore throat
	9	Dyspnoea, sore throat
	10	Chest pain, choking spells
	11	Tired
	12	Tired
	13	
	14	Tired, dyspnoea
	15	Tired, dyspnoea
	16	Tired, dyspnoea
	17	Chest pain, severe dyspnoea
	18	Chest pain, severe dyspnoea
	19	Chest pain, tired
	22	Chest pain, dyspnoea, weakness
	23	Chest pain, dyspnoea, weakness
	24	
	25	Chest pain, dyspnoea
	30	Chest pain, dyspnoea
July	3	Chest pain, dyspnoea
	15	Sore throat, dyspnoea
	16	
	17	Tired
	18	Marked dyspnoea
	22	Chest pain, sore throat
	28	Marked dyspnoea
Aug.	5	Marked dyspnoea
	9	Very weak
(G)	10	Expired


A
B
C
D
E
F
G
TEMPERATURE
BAROMETRIC PR
NOV
DEC
JAN 36
FEB
MCH
APR
MAY 36
JUNE
JULY
AUG
M.B.
RR
SBP
PR
DBP
BLOOD PR.
CO2
pH
LEUCOCYTES
% POLY
90%
80%
70%
1
2
3
4
5
6
7
8
9
10
12



TEXT FIG. 15. Biometeorogram of tuberculosis subject 3. See text for detailed description

Seven episodes have been selected for discussion, because obviously a complete analysis would be interminable. These seven episodes have been indicated by vertical lines with circled markers and lettered **(A)**, **(B)**, **(C)**, **(D)**, **(E)**, **(F)** and **(G)**. These have been selected to illustrate particular phases, primarily major and obvious environmental blows that ultimately resulted in the collapse of resistance and the death of the patient.

The first **(A)** on February 6, when the patient first complained markedly of chest pain and dyspnoea.

The second **(B)** on February 21, when the patient complained of chest pain, a chill and dyspnoea.

The third **(C)** on March 12, when the patient complained of abdominal pain and vomited. Two days previously there had been chest pain and palpitation, and on the day preceding chest pain and pruritus.

The fourth **(D)** on April 10, with chest pain.

The fifth **(E)** on May 1, preceded by three days of chest pain, marked cough, dyspnoea, etc.

The sixth **(F)** on May 14, again associated with chest pain and vomiting, and the terminal episode **(G)** at which time the patient died.

When we survey the general graph for the three months (November, December and January) before the first episode **(A)** we note the characteristic decline of environmental temperatures, the severe cold waves toward the end of December and the beginning of a second severe period of cold at the end of January, 1936.

The oxidation of the skin, as indicated by the methylene-blue time had increased to the 1st of December and remained fairly high **(2)**.

The respiratory rate **(3)** had fluctuated widely and ascended sharply after the cold wave of December; the lowest rate for the entire period was observed on December 4.

The pulse rate **(4)** had remained fairly low until after the December cold wave and then continued between 90 and 100 (morning reading).

The blood pressure levels **(5)** to **(6)** had remained fairly high, with a pressor crest on December 30 and 31 and the diastolic pressor levels remained generally over 60.

Of great significance, the pH level **(8)** had gradually declined from the autumnal highs of 7.67 on November 14 to a low of 7.40 when our first episode is selected.

The leucocyte level had declined **(9)**. Occasional eosinophils were present **(11)**.

Temperatures had remained fairly constant during November and December; with January an increase became evident **(14).**

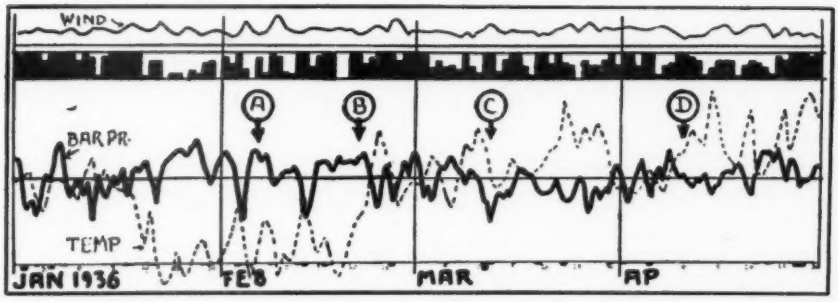
Cholesterol levels **(15)** had remained fairly high (between 130 and 180).

With the end of December the sputum volume began to increase and remained well over 300 cc. per day **(19).**

On the whole the patient's symptoms were not exaggerated during this time and in general we can regard the picture as one that was reasonably stationary.

We now turn for an examination of the weather for the first four episodes which we have had under consideration.

It will be observed from the small meteorogram (text figure 16) that



TEXT FIG. 16. Meteorogram to illustrate environmental conditions at selected periods of the biometeorogram **(A), (B), (C)** and **(D)** in tuberculosis subject 3.

subzero weather began on January 22, 1936 and continued more or less constantly until the 20th of February.

The episode **(A)** was dated at a barometric crest, with minimal temperatures on February 5. A blizzard had preceded on the 3rd and 4th, with high wind velocity on the 9th of the month.

Then followed a series of subzero days.

Two weeks later episode **(B)** was initiated. Here a barometric crest was evident, the temperatures were already rising and finally an unusually and unseasonal high environmental temperature was reached on the 14th.

This was followed by a period of meteorological turbulence with marked barometric and temperature fluctuations.

Episode **(C),** occurring on March 12, was associated with a polar front following the severe precipitation of more than an inch on the 11th, with sharply falling temperatures.

Episode **(D),** on April 10, involved a minor polar front and a secondary (and summating) event after the great barometric crest of the 8th of April. With this the patient revealed a maximum systolic pressor crest.

Episode **(E),** on May 1, involved a minor polar episode at a time when spring high temperatures were in evidence. This particular episode had been preceded by severe precipitation. At this time the minimal diastolic pressor level and the tuberculin reaction began to decline.

Episode **(F),** on May 14, reflects a polar episode and with this there was a major decline in the blood pH.

The final episode **(G),** on August 10, the death of the patient, occurred with the passage of a polar front.

We now return to an analysis of the patient's progress:

The patient, as we have noted, had remained in a fairly stable clinical condition, though the pulse rate had increased somewhat during January and the pH level had declined progressively, as is normal.

With episode **(A)** a date has been selected presenting the period when the first "break" occurred which led to the final decline. This episode was followed by a low pH level.

The pressor crests on January 30 and February 4 were not yet followed by a marked decline in the diastolic blood pressure, that is, resistance was still relatively high.

The body temperature did not rise markedly and the sputum volume actually declined, but the degree of organic upset is evident in the change in electrical resistance.

With episode **(B)** we now observe a sharp febrile reaction. A leucocyte crest follows on the 25th and there is a decline of the diastolic blood pressure with its maximum on the 28th. Sputum increase followed on March 1. The blood pH declined to a low on the 27th of the month and electrical resistance fluctuated widely.

With episode **(C)** citrates had been given in relatively large doses to aid in maintaining a higher pH level and with the next episode the effect was apparent. We observe a pH crest, a febrile crest, sputum volume increased to a maximum on March 23. The COD (exudative phase) reached a summation, with low diastolic blood pressure, high CO_2 content of the blood, at a time when we had high environmental temperatures.

With episode **(D)** a date had been selected when a high systolic pressor crest was in evidence. It was associated with a febrile rise and this in

turn was followed by a high respiratory rate and a high leucocyte count. Sputum volume was transiently diminished, severe chest pain was noted.

With episode **(E)** we note the first severe decline in pressor levels, with an unusually low diastolic of less than 40 mm. Now the tuberculin reaction began to decline, electrical resistance showed maximal variation, sputum volume reached a crest and blood pH was very low. A febrile reaction reached a maximum about ten days later. This occurred during a time when environmental temperatures rose rather abruptly.

With episode **(F)** the final chemical and clinical break occurred and is indicated in a marked and persistant decline in pH levels which occurred with this polar episode. From this date pulse rate increased while the blood pressure fell progressively, cholesterol values reached a low and weight, which had been rather steady for the two preceding months, began its terminal decline.

With episode **(G)** exhaustion became evident with the period after July 10, when environmental temperatures had reached their maximum. After the reactional crest (evident in leucocyte count, blood pressure, etc.) associated with the passage of colder air masses, the respiratory rate, the temperature, the blood pressure, the leucocyte count, all declined. The patient died with the passage of a succeeding polar episode.

The Postmortem Diagnosis

1: Chronic fibrocaseous pulmonary tuberculosis.
2: Dense bilateral pleural adhesions.
3: Brown atrophy of the myocardium.
4: Diffuse lymphoid hyperplasia involving the tracheobronchial, celiac and mesenteric lymph nodes.
5: Atrophy of the liver.
6: Moderate atherosclerosis of the aorta and coronary arteries.
7: Emaciation.
8: Tuberculous adenitis.

DISCUSSION

In this case it has been possible to follow the clinical onset as the various recorded episodes are related to the weather of the time. In each instance the effects of the marked or unusually sudden passage of cold air masses could be related. Furthermore the effect in lessening of resistance at periods of lower pH levels in the population at large, or in the control individuals, was established.

In the comprehensive biometeorogram several clinical episodes have been superficially selected for detailed discussion. These revealed the characteristic biochemical alterations that are reflected in subjective as well as objective clinical evidence of progression (pain, increased cough, gastrointestinal disturbance, fatigue, etc.) which in turn are the end result of meteorological alterations which have conditioned the patient.

The patient was in a fairly stable clinical state at the time of the first zero cold wave in late December, 1935. With the relative anoxia associated with the great pressor crest of the 31st of December, undue metabolic stimulation followed and the fever level, sputum volume, respiratory rate all increased; this was then augmented with the great cold wave of January and February (episodes **(A)** and **(B)**) and can be followed in each of the subsequent events. A catastrophic decline in the pH levels became evident at **(F)** (despite alkalinization). This was associated with the final collapse of resistance (note level of tuberculin reactions).

Death on August 10 followed two days in the wake of a barometric crest.

(To be concluded in next issue)

CELLULAR REACTIONS TO FRACTIONS FROM TUBERCLE BACILLI[1]

FLORENCE R. SABIN

The program of the Committee on Medical Research of the National Tuberculosis Association, under the Chairmanship of Dr. William Charles White, has been based on a renewed coöperative search for the material in the tubercle bacillus which is responsible for increasing the resistance of the body to the disease. That such material exists has been proved by the enhancement of resistance by means of heat-killed tubercle bacilli (1 to 4), as well as by living virulent (5) or attenuated tubercle bacilli, BCG (6).

The basic plan of the Committee has been to select standard strains of tubercle bacilli, to have them grown on synthetic media without protein and then analyzed chemically. The different chemical fractions were to be tested biologically in an effort to trace, first, their rôle in the pathology of the infection and, second, their effect on the course of the disease. These biological studies represent the combined work of a group in my department over a term of years.

In general, every cellular reaction recognized in the lesions of the disease tuberculosis can be reproduced by fractions isolated from tubercle bacilli but none of the fractions thus far studied has brought about any change in resistance to the disease. The materials studied were lipids, polysaccharides and proteins. Since this is a report on a specific program, no attempt is made to cover the basic literature of the general subject.

LIPIDS

The lipids tested in this laboratory are indicated in chart 1 (7[2]), representing the isolations made by Dr. R. J. Anderson of Yale University. It sets forth the results of his work in the simplest possible outline, that is, only the end-products of his extractions. All of the materials enclosed by double lines are acid-fast; those enclosed by single

[1] From the Laboratories of The Rockefeller Institute for Medical Research, New York, New York.

[2] This article contains a complete bibliography on Dr. R. J. Anderson's analyses and the biological studies to date.

lines are non-acid-fast. The most interesting of the lipids from a biological point of view proved to be the phosphatide because it reproduced the

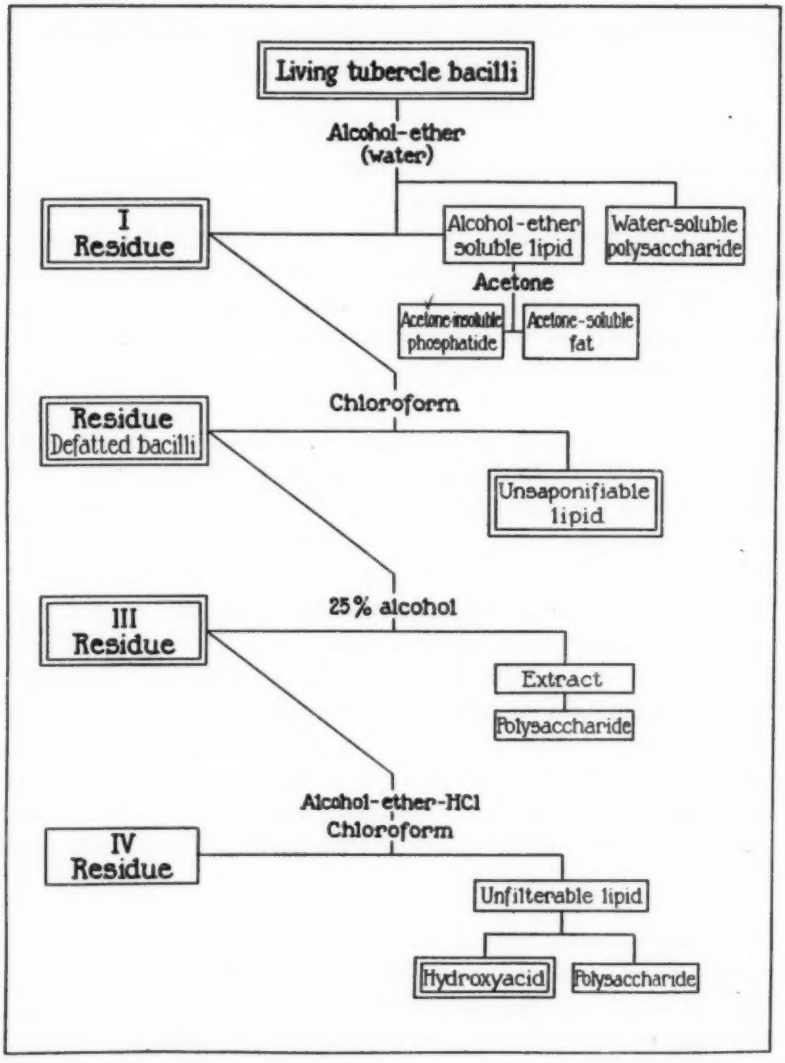


CHART 1

lesion most characteristic of the disease, namely, the tubercle. The phosphatide is a crystalline lipid (8) which is hygroscopic. When it takes up water, it swells and resembles degenerating myelin sheaths of

medullated nerves. Because of this hygroscopic property, uniform suspensions of the lipid can be made in water, thus making biological testing simple; and through its myelin-like appearance, it can be identified within the cells which phagocytize it. The phosphatide is phagocytized by monocytes which, in dealing with it, become epithelioid cells which are usually arranged in tubercles similar to the hard tubercles of the actual disease.

By means of a study of the living cell in its reaction to neutral red, an epithelioid cell can be more precisely defined. Vital neutral red does not stain the basic cytoplasm as long as the cell is alive, but only certain granules in the cytoplasm and the fluid of the cellular vacuoles of digestion. An epithelioid cell is a phagocytic mononuclear—a monocyte in which these vacuoles have been so increased in number and so reduced in size that the whole centre of the cell, appearing as a large rosette in the supravitally stained form, is uniformly dense in fixed tissues. An epithelioid cell is therefore a cell which has phagocytized some material which it has dispersed into exceedingly fine particles. The monocyte deals thus with tuberculo-phosphatide. The large rosette of vacuoles around the centrosome has a tendency to restrict cell division but not nuclear division, giving rise to the epithelioid giant cell (8, 9). There is no evidence that the epithelioid cells dealing with phosphatide return to the state of the original monocyte; rather, in our experiments, after a long interval they died either singly (10) or *en masse*, simulating caseation (8). It may therefore be that some intermediate product of the degradation of the phosphatide is toxic to the cell.

In his analysis of the phosphatide, Doctor Anderson found two hitherto unknown fatty acids which he named tuberculo-stearic acid and phthioic acid. In the phthioic acid resided all of the power of the phosphatide to induce the formation of tubercles (8). Thus the cellular reaction to the phosphatide is the production of epithelioid cells.

WAXES

The property of acid-fastness in the bacilli is due to certain wax-like materials which Doctor Anderson has shown to be higher hydroxy-acids, first designated as unsaponifiable wax and later given the name mycolic acid. They are highly stable chemical compounds but the cells are able to degrade them, albeit very slowly. They were introduced into the tissues either as a dry powder or in specially prepared suspensions (11). In either case the material was presented to the cells in aggregates of

such size as to induce the formation of multiple-cell giant cells. That is to say, monocytes, often a hundred or more, fused and by a membrane of their pooled surface films phagocytized the wax (12). Within these giant cells the wax soon lost its property of acid-fastness; it was broken up to some degree into finer particles and eventually became so degraded that the giant cell fell apart into its constituent normal monocytes. Both types of giant cells, the one with a few peripheral nuclei and cytoplasm of the epithelioid type, and the large multicellular one, are characteristic of tuberculosis. The wax, then, induces the formation of foreign body giant cells.

POLYSACCHARIDES

In our tests tuberculo-polysaccharides were employed which had been given to us by Doctor Anderson and by Dr. Michael Heidelberger of the College of Physicians and Surgeons of Columbia University. Doctor Heidelberger gave us also highly purified polysaccharide from pneumococcus Type I and we received pneumococcus Type III polysaccharide (13) from Dr. Walther Goebel of the Rockefeller Institute. The tuberculo-polysaccharides were all acid. They proved to be entirely nontoxic to both normal and tuberculous animals (13). They were excreted by the kidneys. Both simple sugars, such as glucose and trehalose, as well as bacterial polysaccharides of different structure, showed one constant cellular reaction. When injected into the tissues they attracted neutrophilic leucocytes from the vessels. This action was immediate because the fall in neutrophils in the blood occurred within ten minutes; this phenomenon was shown to be true for other stimuli by Beard and Beard (14). Following intraperitoneal injections of the sugars it was found in our laboratory that the neutrophils drawn into the peritoneal cavity were replaced by young forms from the marrow in from one to six hours. During this entire period the neutrophils extravasated into the peritoneal cavity remained alive and active. This observation indicates that the injected sugar, reaching the sinuses of the marrow, was probably the chemotactic agent which called the cells from the marrow to the vessels. At the end of twenty-four hours the extravasated neutrophils had aged and become so damaged that they were being phagocytized and digested by macrophages. This reaction was completed within forty-eight hours. Through repeated daily injections of tuberculo-polysaccharide a normal blood count was maintained by means of a hyperplastic marrow, indicating that the products of the digestion of

extravasated neutrophils were the stimulus for cell division and maturation in bone marrow (13). Thus the polysaccharides produce only one cellular reaction, namely, a chemotactic effect on neutrophils.

TUBERCULO-PROTEINS

The proteins employed in these studies were prepared from the bacilli by Doctor Heidelberger and from the media on which the bacilli had been grown by Dr. Florence Seibert of the Henry Phipps Institute. We received protein also from Dr. John Reichel of Sharp and Dohme. The proteins were tested in three forms, that is, in solution, in suspensions of freshly made precipitates and in highly insoluble particles (15). It may be assumed that the protein liberated in the infection itself is usually in soluble form; while it may become precipitated in the body, it would never occur in the highly insoluble form that can be produced by means of acid reagents. The cellular reactions were the same in kind in the tuberculous and in the normal animal but in every respect greatly intensified in the former. The immediate reaction from the injection of any form of protein into the tissues was the extravasation of neutrophils into them. This was true also, although in less degree, for all the menstrua used, distilled water or saline. The specific effect of the proteins was an increase in monocytes. When given in solution in a normal animal, this increase was the only effect noted; in tuberculous animals a few monocytes were stimulated and an occasional epithelioid cell was found. Freshly precipitated tuberculo-protein gave rise to many monocytes and a few epithelioid cells in normal animals and to many tubercles in tuberculous ones. Thus it becomes clear that the protein contains materials which, when phagocytized as particulate matter, can induce the formation of the epithelioid type of cell. The highly insoluble forms of the protein proved to be marked cellular stimulants, giving rise to every form of phagocytic mononuclear cell—monocytes, stimulated monocytes, macrophages, epithelioid cells and both types of giant cells (15). All these reactions were intensified in tuberculous animals. Besides the induction of monocytes, Miller (16) found that repeated intraperitoneal injections of tuberculo-protein in solution gave rise to plasma cells.

To summarize, the tuberculo-lipids and proteins all induced a new formation of monocytes; the phosphatide changed monocytes into epithelioid cells and their derivative giant cells; the waxes induced the fusion of monocytes into foreign body giant cells; the proteins induced

a more varied stimulation of monocytes, that is, into epithelioid cells, macrophages and both types of giant cells. These reactions were least with the soluble form and most with the insoluble, and in every instance they were intensified in tuberculous animals. The polysaccharides were chemotactic to neutrophilic leucocytes; monocytes were involved only indirectly in that they eventually phagocytized extravasated neutrophilic leucocytes.

SENSITIZATION

It had been thought that sensitization to tuberculo-protein, as expressed by the delayed tuberculin type of skin reaction, could be brought about only by living tubercle bacilli. Then such sensitization was produced by heat-killed tubercle bacilli (1 to 4); and finally the production of tuberculo-proteins that are good antigens extended knowledge of this subject (17, 18, 19). These proteins were obtained by Doctor Seibert (17) from synthetic, protein-free media on which tubercle bacilli had been grown and from the bacilli themselves by Doctor Heidelberger (20, 21, 22). It now appears to be clear that the conflicting results of negative reactions and partial success in sensitizing with certain preparations were due in part to the use of the nonantigenic boiled protein solutions, tuberculin or OT, or to the varying potency of other preparations treated less drastically (17). Seibert, Pedersen and Tiselius (23) have shown that the molecular weight of the fully antigenic protein molecule from tubercle bacilli, human strain, is 32,000, whereas that of tuberculin, OT, is 16,000, and of the purified protein derivative, PPD of Seibert, 9,000.

The power of the tuberculo-protein to induce skin sensitization was markedly enhanced by the addition of tuberculo-phosphatide to the protein (19). Having demonstrated first that phosphatide entirely freed of bacilli does not sensitize to the protein, it was then shown that in the presence of phosphatide less protein sensitizes and does so more quickly, giving rise to larger and more intense reactions with more necrosis. Moreover, these reactions were of the delayed type, becoming maximum at twenty-four hours and fading at forty-eight hours, like the reactions in the actual disease. The action of the phosphatide was to induce tubercle formation.

The sensitization induced by protein differed from the conditions of sensitization or allergy present in the actual disease in certain significant ways. First, an animal sensitized to tuberculoprotein will react to the

same protein, or even to protein from a different strain (17) but not to OT, that is, not to the protein molecule degraded by heat (17, 19, 23). Since the tuberculous animal does so react, it seems certain that there is some element present in the tuberculous and lacking in the normal; that is to say, infection may result in the formation of cellular antibodies with reactive groupings that are lacking in the artificially sensitized animal. Second, an animal sensitized to the protein has not shown any increased resistance to subsequent infection (15, 24), nor has it shown the slightest trace of the Koch phenomenon. Instead its reaction to inoculation with tubercle bacilli has been like that of first infection (19). Third, it has been shown by Rich and Lewis (25) that the connective tissue cells of the tuberculous animal retain their sensitivity to the protein when grown outside the body—as Moen and Swift (26) have demonstrated even after many generations—while the cells of the protein-sensitized animal do not retain this property in tissue culture (27, 28).

From these observations it has been concluded in our laboratory that the type of sensitization which can be induced by tuberculo-protein is only one phase of the reactions that are set up by the infection and is no part of the changes which are expressed in altered resistance.

THE MECHANISM OF ANTIBODY FORMATION

The phosphatide and the waxes exhibited properties that enabled one to identify them within the phagocytic cells—myelin figures in the case of the former and acid-fastness in the latter. In order that such an advantage might be made available for cellular reactions to protein, Doctor Heidelberger kindly furnished for our studies a dark red dye-protein, R-salt-azo-benzidine-azo-egg albumin, which he had found to be a good antigen. He had observed that intravenous injection of this antigen brought about a higher antibody titre than injection by other routes. When injected intravenously, it was phagocytized by the Kupffer cells of the hepatic sinuses and the macrophages of the splenic pulp. The neutrophils aided the macrophages in some measure by taking up the dye-protein and bringing it to them. When injected intraperitoneally, the dye-protein was taken up by local macrophages and by the endothelium of regional lymph nodes; when intracutaneously, by the macrophages of the dermis and the endothelium of regional lymph nodes. It became clear that a much greater amount of dye-protein was retained locally after intracutaneous than after subcutaneous injection. Moreover, repeated, small injections brought more cells into action than one

injection of a large dose. After an interval of from four to seven days, the cells which had phagocytized the dye-protein presented an accentuation of the property which had caused Ranvier to give to them the name "clasmatocyte," namely, an extensive liberation of parts of their surface films. By this time the phagocytized dye-protein had disappeared and it has been assumed by us that the antigen had entered the cytoplasm of the cells, stimulated the formation of globulin, and converted some of the latter into antibody globulin. These globulins were contained in the cytoplasm and then set free from the surface of the cells. The finding of antibodies in the serum coincided in time with the cellular phenomenon just described.

The observations reported above bring more evidence to bear on the concept that the cells of the reticulo-endothelial system are involved in the production of globulin, both normal and the immunologically reactive form, antibody.

We picture a functional unity in the phagocytic mononuclear cells, the monocyte, macrophage, epithelioid cell, both types of giant cell and the so-called specific phagocytic endothelia—in other words, in the reticulo-endothelial system.

Cellular and immunological reactions in tuberculosis centre around the functions of the monocyte.

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BILATERAL TUBERCULOUS PLEURAL EFFUSIONS[1]

A Study of 45 Cases

ALFRED L. PAINE

Bilateral tuberculous pleural effusion has been only occasionally recorded in the literature and most reports deal with isolated cases. This is no doubt due to the rarity of the condition, but it also indicates that no special significance has been attached to the occurrence. Moreover, in almost all cases reported the patients were receiving pneumothorax on one side. Thus Als (1) in 1920 first reported an instance of bilateral effusion in a pneumothorax patient. Soon after, Fishberg (2) reported another and Peters (3) in 1925 reported 3 cases and gathered together 20 others from the literature, all of whom were undergoing pneumothorax treatment on one side.

These writers were mainly concerned with the bilateral pleural effusion as a complication of pneumothorax treatment. However, Wilson (4) in a recent report on 14 cases included 9 in whom pneumothorax was not present It is interesting to note, though he draws no conclusion therefrom, that in a number of his cases tuberculosis eventually developed elsewhere than in the lungs, intestines and larynx. The various organs mentioned were the pericardium, peritoneum, spine, kidney, knee and eye. In 10 of his 14 cases effusion occurred in the presence of extensive pulmonary tuberculosis, a fact that no doubt obscured the rôle of bilateral pleurisy as a possible omen of the impending outbreak of disease elsewhere. In any event he makes no mention of its prognostic significance. Hurrell (5), Burrell (6) and Rubin (7) report single cases where they do recognize the seriousness of its import.

THE PRESENT SERIES

It has recently been noted at Manitoba Sanatorium that bilateral pleural effusion without artificial pneumothorax seems to have become more common; also that it has a distinctly graver prognosis than unilateral effusion. The series of 45 individuals presented herewith com-

[1] From Manitoba Sanatorium, Ninette, Manitoba, Canada.

prises all such cases of bilateral effusion observed in the last twenty years and it should be repeated that in none was pneumothorax present. Of these, 16, or 36 per cent, fall within the last five years' period. The writer hopes to point out that bilateral effusion is not merely an effusion on two sides but is often, indeed usually, a manifestation of widely disseminated infection in an individual possessing at times unusual powers of resistance but all too often eventually developing multiple foci of disease.

Diagnostic criteria: All the patients in the group had pleural effusion, presumably tuberculous, affecting both sides either simultaneously or alternately and uncomplicated by pneumothorax. The minimum diagnostic requirement was the presence of effusion at both bases as demonstrated by X-ray and a clinical course in keeping with a diagnosis of tuberculous pleurisy which led to admission to the Sanatorium. In addition, of the total group of 45, fluid was obtained on aspiration in 30 and in 13 of these on both sides. Tubercle bacilli were found in the aspirated fluid in 8, which is admittedly a low percentage. However, in 22, bacilli were isolated sooner or later from some part of the body. In 31, diagnosis was supported either by finding tubercle in the fluid or eventually in sputum or by the development of undoubted tuberculosis in some other organ.

In some of the cases who did well the diagnosis could not be definitely proved because they recovered without aspiration or attempts to isolate the tubercle bacillus from aspirated fluid failed. However, in those who developed complications, and this is the significant group, the aetiology was proved sooner or later by the course of the disease.

Prognosis compared to that of unilateral effusions: Before making a detailed analysis of the course of these patients with bilateral effusion some definite indication should be given of the greater seriousness of this condition as compared to unilateral effusion. It seems worth while to compare the course of those with slight or no lung lesions at onset of effusion who had adequate Sanatorium treatment with a similar group of unilateral effusions reported by Trudeau (8). The group thus selected, as shown in table 1, comprises 27 individuals followed over a period of one to nineteen years as against Trudeau's series of 83 observed from three to twenty-five years. End results in Trudeau's series might be considered too good to afford a suitable basis for comparison as he found that only 14 per cent suffered relapse. However, most tuberculosis workers look upon unilateral effusion with slight or no lung involvement as a relatively benign condition when adequately treated and would expect a

much better prognosis than when more advanced lung lesions are present. Considering pleural effusions as a whole it should be noted that Burrell (9) anticipates 40 per cent to be eventually followed by active pulmonary tuberculosis.

As seen in table 1 the percentage of those with relapse in the bilateral series is four times as great as in the unilateral group and, of those with relapse, 44 per cent developed tuberculosis in organs other than the lung, whereas Trudeau makes no mention of extrapulmonary tuberculosis occurring in his group. It will also be seen that end results are distinctly worse for the bilateral series. Percentages show five times as many dead as in the unilateral group and only slightly more than half as many well. In the bilateral series all deaths were due to tuberculosis while cause of death is not stated in the unilateral series. Also in the bilateral group

TABLE 1

Comparison of prognosis in unilateral and bilateral effusions in those with slight or no lung lesions at onset of pleurisy

SERIES	NUMBER OF CASES	INCIDENCE OF RELAPSE				PRESENT STATUS					
		Total		Nonpulmonary		Well		Living		Dead	
		Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Trudeau—unilateral	83	12	14	—	—	74	89	4	5	5	6
Present series—bilateral	27	15	56	12	44	13	48	6	22	8	30

of the 6 tabulated as living, all are under treatment, 3 with tuberculous nephritis, one with progressive pulmonary disease, one with Pott's disease and the other still clear of complications at one year from onset. Thus prognosis in the group under treatment could not be considered good. Comparative data for those called living in the unilateral series are not available.

Extent of pulmonary disease at onset in relation to subsequent course: Returning to analysis of the present group, it is seen in table 2 that, contrary to previously reported series, the majority of the patients had little or no pulmonary involvement at onset, being admitted for pleurisy rather than pulmonary tuberculosis. In spite of this, the group as a whole showed a marked tendency to develop subsequent tuberculous complications and to ultimately do badly. Thus, in 47 per cent pul-

monary disease appeared or increased while in 38 per cent tuberculosis involved other organs. In some instances both pulmonary and nonpulmonary disease appeared in the same individuals so that of the whole group 56 per cent showed further manifestations of tuberculosis and 44 per cent have so far remained free. As to present status, 47 per cent are well, 22 per cent are under treatment and 31 per cent are dead.

Again referring to table 2, it will be noted that those with no apparent pulmonary disease at onset had a higher percentage of subsequent complications than those with pulmonary lesions, even including the ad-

TABLE 2

Relation of extent of pulmonary disease at onset of pleurisy to subsequent tuberculous conditions and to present status

LUNGS AT ONSET	NUMBER	PER CENT	TUBERCULOUS LESIONS FOLLOWING PLEURISY						PRESENT STATUS					
			Lungs*		Other organs†		Total‡		Well		Under treatment		Dead	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
No apparent disease	24	54	14	58	12	50	18	75	6	25	9	37.5	9	37.5
Suspect	5	11	0	0	0	0	0	0	5	100	0	0	0	0
Minimal	10	22	3	30	2	20	3	30	8	80	0	0	2	20
Far and moderately advanced	6	13	4	67	3	50	4	67	2	33	1	17	3	50
Total	45	100	21	47	17	38	25	56	21	47	10	22	14	31

* Lungs: Indicates new disease or increase in previous disease.

† Other Organs: Does not include larynx or intestines.

‡ Total: Refers to individuals rather than lesions, some patients having both pulmonary and nonpulmonary tuberculosis.

vanced group. Also, prognosis for those with apparently clear lung fields at onset, as indicated by present status, is not as good as for the whole group nor is it materially better than for the advanced group in which the 3 deaths were actually due to extensive pulmonary disease present before onset of pleurisy. In other words, for reasons to be suggested later, the outlook of patients with bilateral pleurisy hinges on less tangible factors than manifest pulmonary disease at onset.

Frequency of involvement of many organs: As stated above, in 17, or 38 per cent of the whole group, tuberculosis eventually developed in organs other than the lungs. The organs affected and the incidence were

as follows: peritonitis 7; pericarditis 2; meningitis 3; Pott's disease 5; hip disease 1; tuberculosis of mandible 1; nephritis 5; salpingitis 4; inguinal adenitis 2; sternal adenitis 1; supraclavicular adenitis 1; otitis media 2; addison's disease 1; tuberculosis of liver 3; tuberculosis of spleen 2. Multiple foci in a single individual were common and it should be stated that 5 of the patients thus affected developed typical miliary pulmonary tuberculosis. These factors point to widely disseminated infection. It has become a dictum that we must watch for pulmonary tuberculosis after a unilateral pleurisy; it would seem from the present

TABLE 3

Relation of age to course of disease

AGE GROUPS	NUMBER	PER CENT	TUBERCULOUS LESIONS FOLLOWING PLEURISY						PRESENT STATUS					
			Lungs*		Other organs†		Total‡		Well		Under treatment		Dead	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
15–24	24	53	9	38	7	29	11	46	14	58	5	21	5	21
25–34	12	27	7	58	6	50	8	67	4	33	4	33	4	33
35–44	5	11	4	80	3	60	5	100	0	0	1	20	4	80
45–59	4	9	1	25	1	25	1	25	3	75	0	0	1	25
All ages.....	45	100	21	47	17	38	25	56	21	47	10	22	14	31

* Lungs: Indicates new disease or increase in previous disease.

†Other Organs: Does not include larynx or intestines.

‡ Total: Refers to individuals rather than lesions, some patients having both pulmonary and nonpulmonary tuberculosis.

series that one must be equally alert for nonpulmonary tuberculosis following bilateral pleurisy.

Relation of age to course of disease: Table 3 shows the incidence of bilateral pleurisy in the various age groups; also the relation of age to the development of tuberculous complications and to present status. It will be seen that over half the patients were in the decade of fifteen to twenty-four. It is difficult to estimate the influence of age on the course of disease, as the older age groups are too small to yield dependable statistics. However, one may say that all age groups up to sixty were affected and all showed both pulmonary and nonpulmonary complications.

Relation of sex to course of disease: Table 4 shows that more females

were affected than males; 58 per cent as against 42 per cent. On the other hand the males had a higher incidence of complications, a higher mortality rate and a greater percentage still under treatment.

Interval between effusions as a factor in course of disease: Fluid occurred first 13 times on the right side and 19 times on the left side while in 13 cases it was present on both sides when first seen. In the latter group it appeared most unlikely that fluid always developed at exactly the same time on each side. For this reason all effusions which were present on both sides at any one time were grouped for study under the heading of concurrent rather than simultaneous. It seemed reasonable to expect that more complications and a worse outlook would be found in

TABLE 4

Relation of sex to course of disease

SEX	NUMBER	PER CENT	TUBERCULOUS LESIONS FOLLOWING PLEURISY						PRESENT STATUS					
			Lungs*		Other organs†		Total‡		Well		Under treatment		Dead	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Male	19	42	9	47	9	47	13	68	6	32	5	26	8	42
Female	26	58	12	46	8	31	12	46	15	58	5	19	6	23
Total	45	100	21	47	17	38	25	56	21	47	10	22	14	31

* Lungs: Indicates new disease or increase in previous disease.

† Other Organs: Does not include larynx or intestines.

‡ Total: Refers to individuals rather than lesions, some patients having both pulmonary and nonpulmonary tuberculosis.

those with the shortest interval between effusions, so the group was studied with this in mind.

Effusions were concurrent in 21, or 47 per cent of the whole group. In 15, or 33 per cent, the interval between onsets of effusion was less than one year while in the remaining 9, or 20 per cent, the interval was over one year. The figures in table 5 indicate that those with concurrent effusions had a somewhat higher incidence of complications in all sites and a higher mortality rate than the other subgroups. However, the difference is not as marked as one might expect. Furthermore, there was actually a higher percentage of nonpulmonary complications in the group with over a year between effusions than in the concurrent group.

One is impressed with the fact that the pathogenic factors that bring about these complications may operate over a considerable period of time.

Length of treatment as a factor in prognosis: As in unilateral effusions it might be expected that adequate length of treatment of the effusion would tend to prevent the development of further tuberculous manifestations and ensure a better ultimate prognosis. Table 6 shows the course of disease of the 39 who had slight or no pulmonary disease according to length of treatment. It will be seen that pulmonary tuberculosis developed more often in the group with shorter treatment but that there was a higher incidence of nonpulmonary complications in the group that

TABLE 5

Interval between onsets of effusion in relation to course of disease

INTERVAL BETWEEN ONSETS OF EFFUSION	NUMBER	PER CENT	TUBERCULOUS LESIONS FOLLOWING PLEURISY						PRESENT STATUS					
			Lungs*		Other organs†		Total‡		Well		Under treatment		Dead	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Concurrent.....	21	47	12	57	8	38	14	67	8	38	4	19	9	43
One year or less...	15	33	5	33	5	33	6	40	8	53	4	27	3	20
Over one year....	9	20	4	44	4	44	5	56	4	45	3	33	2	22
Total.....	45	100	21	47	17	38	25	56	21	47	10	22	14	31

* Lungs: Indicates new disease or increase in previous disease.

† Other Organs: Does not include larynx or intestines.

‡ Total: Refers to individuals rather than lesions, some patients having both pulmonary and nonpulmonary tuberculosis.

had longer treatment and that the total complications were also greater in this group. There is little to choose in the present status of the two groups, though the longer treated group has relatively more dead and less well but fewer still under treatment for subsequent tuberculous complications. In summary, in this series one could not claim the expected advantage in prognosis for the longer treated group. The group is small for reliable conclusions but other factors are in operation. Those longer treated were usually sicker on admission so could be expected not to do so well. Five of the 27 in the longer treated group developed some other form of tuberculosis within the four-month period, and further treatment was for this rather than the pleurisy. Also, though it is

no argument against adequate treatment, the pathological sequence behind bilateral effusions tends to progress regardless of all efforts to arrest it and hence response to treatment is less striking than in unilateral effusion.

Prognosis in general: The analysis thus far has served to emphasize the unhappy outlook for those with bilateral effusion. What signs may we discover that foretell a favorable outlook? Unfortunately, such are all too few. It appears that apparent absence of lung disease at onset is not necessarily a good omen, nor is there anything in the nature of, or interval between effusions that offers a favorable forecast. The only obvious ally is time. Thus of the 16 people who managed to stay clear

TABLE 6

Prognosis in relation to length of treatment in those with slight or no lung lesions at onset of pleurisy

LENGTH OF TREATMENT	NUMBER	PER CENT	TUBERCULOUS LESIONS FOLLOWING PLEURISY						PRESENT STATUS					
			Lungs*		Other organs†		Total‡		Well		Under treatment		Dead	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
4 months or over	27	69	11	41	12	44	15	56	13	48	6	22	8	30
Under 4 months	12	31	6	50	2	17	6	50	6	50	3	25	3	25
Total	39	100	17	44	14	36	21	54	19	49	9	23	11	28

* Lungs: Indicates new disease or increase in previous disease.

† Other Organs: Does not include larynx or intestines.

‡ Total: Refers to individuals rather than lesions, some patients having both pulmonary and nonpulmonary tuberculosis.

of tuberculous complications for five years all but one are well. The exception is a woman, age twenty on admission, who six years after her pleurisy became psychotic and three years later developed pulmonary tuberculosis of which she died.

Prognosis for the group who developed tuberculous conditions after effusion is naturally worse than for the whole series. Thus, of this group of 25, only 2, or 8 per cent, are well, 9, or 36 per cent are still under treatment and 14, or 56 per cent are dead. It is significant that the appearance of subsequent tuberculous manifestations occurred in most cases within two years of onset of the first effusion. Thus 20, or 83 per cent, showed further disease within two years and 11, or 46 per

cent, within six months. These people often showed good temporary resistance, at times arresting their tuberculosis in one or more sites only to have a fresh focus of disease appear in some organ. This and other features of interest are illustrated in the case reports.

CASE REPORTS

Case 27: M. S., a graduate nurse, age twenty-four, gave no history of contact except in her work, and a routine chest film in 1932 showed no evidence of tuberculosis. She was admitted in September, 1934 with a left-sided pleural effusion which did not require aspiration, but three months later an X-ray film showed fine miliary shadows throughout both lungs as well as a residual effusion at the left base. Parenchymal shadows cleared rapidly, but in March, 1935 a large effusion developed on the right side which was aspirated twice. Bacilli were not found on smear or culture. She made a good recovery and left in September, 1935 with X-ray examination showing fluid resorbed on both sides and lung fields apparently cleared.

Beginning in February, 1936 several lumps appeared at intervals over the sternum; two were excised leaving persistent sinuses. In January, 1937 she developed lower back pain radiating to left lower abdomen and that spring had a subtotal hysterectomy with left tube and ovary removed. These operations were done elsewhere and there is no report of findings. Pain persisted in back and lower abdomen and began to radiate down the right leg. She attended a tuberculosis clinic where advanced Pott's disease was discovered and she was readmitted in August, 1937. She failed rapidly, developing meningeal symptoms a few weeks after admission, and died in coma.

Spinal fluid showed 950 cells, chlorides 587 mg., no sugar, positive globulin test. At autopsy the significant gross findings were: sinuses over the sternum, some injection of pelvic peritoneum, calcified nodules in apices of both lungs, Pott's disease with destruction of the twelfth thoracic vertebra and part of the first lumbar and a large psoas abscess. Microscopical section showed early tuberculous meningitis; tuberculosis of adrenals and tuberculous tissue from the sinuses over the sternum which were no doubt due to breaking down of sternal lymph nodes.

Remarks: Onsets of effusion were six months apart and during the interval the patient developed miliary lung disease. She recovered well but within six months tuberculous disease again manifested itself, first in sternal lymph nodes, then in spine and finally in meninges from which she died. Adrenal insufficiency may also have been partly responsible for death in view of autopsy findings.

Case 34: P. T., a Ukrainian farmer, aged forty-one, developed right-sided pleural effusion in February, 1936. Prior to this, one sister had tuberculosis and an X-ray film taken because of contact in 1932 showed no evidence of tuberculosis. Fluid was aspirated twice in General Hospital and he was admitted to this Sanatorium in June, 1936 partly for pleurisy, but mainly because of a painful back. Pott's disease was suspected and he was on fracture boards for several months, but X-ray films of the spine were always negative. He was discharged after four months' treatment and remained fairly well until fourteen months later when he was readmitted with greatly enlarged fluctuant right supraclavicular lymph nodes, large pleural effusion on the left side and marked ascites. His condition became rapidly worse and he died twenty days after admission, terminal symptoms being meningeal.

Sputum was always negative but bacilli were found in both pleural and peritoneal fluid, in pus from cervical nodes and from the ear. Autopsy findings in summary were: tuberculosis of cervical, mediastinal and preaortic lymph nodes, left pleural effusion, tuberculous enteritis and peritonitis and miliary tuberculosis in liver, spleen and kidneys. Permission to open the skull was not granted.

Remarks: The interval between onsets of effusion was twenty-three months. There was no evidence of pulmonary tuberculosis at onset. The second effusion was obviously part of the picture of miliary tuberculosis from which the patient died. Considering the subsequent course it seems likely that the first effusion was also a manifestation of haematogenous dissemination.

Case 32: E. W. was a university student, age nineteen, who knew of no contact with tuberculosis, but she became ill with pleurisy in December, 1935. On admission pleural effusion was present at both bases but lung fields appeared clear. Fluid cleared rather slowly but without aspiration. In August, 1936, eight months later, an X-ray film showed fine miliary shadows throughout both lungs which after initial progression largely cleared within a year. Sputum was never positive, but nineteen months after onset a painless discharge from the left ear occurred and bacilli were found in the pus. Bilateral tuberculous nephritis was diagnosed by cystoscopic examination thirty-three months after pleural onset and since then urine has always contained tubercle bacilli. An acute Pott's disease developed three months after the nephritis. Spinal fusion was done. She is still under treatment for the kidney condition. There is no evidence of active tuberculosis in the chest film at present.

Remarks: Points of interest are the bilateral effusion at onset with no apparent lung disease; miliary shadows developing later but clearing; still later tuberculous otitis media, nephritis and Pott's disease.

Case 25: G. C., male, age twenty-three, admitted July, 1934.

Synopsis: Effusion, bilateral at onset in July, 1934 with no apparent pulmonary disease. Bacilli found in pleural fluid. Pott's disease developed six months from onset. Spine graft. Tuberculous nephritis thirty-three months from onset. Left nephrectomy. Well and working five and one-half years after initial pleurisy.

Case 30: J. M., male, age forty-two, admitted September, 1935.

Synopsis: Minimal apparently arrested tuberculosis in 1934. Concurrent bilateral effusion in August, 1935. Miliary lung disease in December, 1935; also caries of mandible, presumably tuberculous with bacilli found in tooth socket. Bacilli also found in sputum and pleural fluid. Died at home November, 1936.

Case 44: W. D., male, age twenty-three, admitted April, 1939.

Synopsis: Right-sided effusion in April, 1939. No apparent pulmonary disease. Left-sided effusion in June, 1939. Extensive miliary lung disease in February, 1940. Sputum negative. Still under treatment.

Case 37: M. R., a female, age twenty-three, admitted March, 1937.

Synopsis: Chest film taken in November, 1936 on routine check-up as a nurse showed no evidence of tuberculosis. Developed bilateral effusion four months later. Aspirated both sides and tubercle bacilli found in fluid. No apparent lung disease. Recovered well and X-ray films showed no evidence of parenchymal disease approximately two years after onset of pleurisy. At home and married three years after onset.

DISCUSSION

A survey of the foregoing case reports and analysis leaves little doubt as to the poor prognosis in bilateral tuberculous effusion. On all counts it would seem to be a distinctly more malignant condition than unilateral effusion. Aside from being followed by a higher percentage of pulmonary tuberculosis, there is a frequency of involvement of other organs seldom seen in unilateral pleurisy. Furthermore, one cannot fail to be impressed with how often not only one but several organs became involved in a single individual and these people not uncommonly (in 5 cases) also had typical miliary lung disease at one time or other during their course. Why are bilateral effusions and not unilateral ones so frequently followed by these multiple foci of disease? Considering the frequency of miliary lung disease and involvement of other organs, such as spine, kidney, adrenals, lymph nodes and meninges, where

the mode of infection is conceded to be through the blood stream one must conclude that bilateral effusion is usually a manifestation of haematogenous infection and not infrequently of generalized miliary tuberculosis. Unilateral effusions on the other hand are generally considered secondary to subpleural lung lesions originating from aerogenous infection.

The assumption that bilateral pleurisy is part of the picture of blood-spread tuberculosis offers an explanation of some of the features observed in the previous analysis. It would explain why the presence or absence of pulmonary tuberculosis at onset of pleurisy, as shown by X-ray films, had no particular bearing on the subsequent appearance of tuberculosis in other organs and also why Sanatorium treatment apparently did not materially improve the outlook.

Other features, such as the considerable interval between onsets of effusion in some instances, are harder to understand and seem to be bound up with the pathogenesis of pleural effusion. It has long been believed that effusions were due to the actual infection of the pleura from a subpleural pulmonary lesion as stated by Boyd (10). However, as far back as 1917 Paterson (11) showed that the production of a pleural effusion in guinea pigs by the injection of tubercle bacilli into the pleural cavity depended on the animal's being previously infected.

The allergic nature of serous effusions was finally proved by Petroff and Stewart (12). They sensitized guinea pigs by employing a killed culture of tubercle bacilli and then injected Old Tuberculin into the peritoneal cavity. A serous effusion occurred not only into the peritoneal cavity but into other serous cavities as well. Howard and DeVeer (13) confirmed these findings regarding the allergic nature of effusions into serous cavities in tuberculosis. They injected Old Tuberculin into the peritoneal cavity or either pleural cavity. With all sites of injection they were able to produce a simultaneous effusion in both pleural cavities and the peritoneal cavity. Pericardial effusion also occasionally developed.

It would therefore seem that bilateral pleural effusion is a manifestation of haematogenous tuberculosis and like all effusions is dependent in some way upon allergy for its production. Rubin (7) in an exhaustive article on haematogenous tuberculosis has pointed out the predilection of this form of tuberculosis for serous membranes. He makes special mention of the pleura as a frequent site but his case reports include only one instance of bilateral effusion. He explains the frequent pleural involve-

ment on anatomical grounds and refers to Snow Miller's excellent work on the anatomy of the lung (14). Miller has demonstrated that the bronchial artery supplies the pleura and the pulmonary artery supplies the subpleural lymphoid tissues. The favorite site for tubercle formation is thus in the subpleural region which is the transitional zone from the bronchial to the pulmonary circulation. Rubin concludes that tubercle bacilli are able to travel by way of the superficial (pleural) or deep (pulmonary) lymphatics to the surface as well as within the parenchyma of the lung.

From the above it is apparent that the pleura has every opportunity to become heavily infected in haematogenous tuberculosis and one would expect pleuritis in some form to be almost invariably present. We have found that pleural effusions in miliary tuberculosis of the lung are relatively common. It is difficult to estimate the incidence because it is not always possible to differentiate miliary tuberculosis as seen in the X-ray film from shadows due to bronchogenic spread. However, in the last ten years, 17 cases considered to be typical miliary tuberculosis of the lung have been admitted. Of these, 10, or 59 per cent, developed effusion and in half of them it was bilateral.

It would seem that the dominant factor in the production of these effusions is allergy. Tuberculotoxin in large quantities must reach the pleura from the pulmonary parenchyma in the same manner as described by Rubin for tubercle bacilli. Also tuberculotoxin is no doubt produced by the tuberculous lesions within the pleura itself. It seems probable that infection in some cases of miliary tuberculosis may forestall this allergic reaction by overwhelming the allergy-producing mechanism and no effusion takes place. On the other hand, it may be supposed that a high degree of allergy is present in other cases along with unusual resistance and in these people effusion will result which may not only be on one side but also bilateral and even involve the peritoneum and pericardium, as in the experiments in allergy already quoted and in case 11 in the present series (see master chart[2]). Because of unusual resistance, some of these cases temporarily recover and miliary shadows in the lung, if demonstrable by X-ray examination, tend to resolve completely, as seen in cases 27 and 32. In others it seems probable that the miliary tubercles retrogress before they reach the stage of caseation necessary for X-ray visualization.

The above explanation is hypothetical and only partially covers the

[2] Copies of this master chart may be obtained from the author on request.

problem. Reasoning along these lines, one is still at a loss to explain the time interval between onsets of effusion in some cases of bilateral pleurisy, or indeed why the allergic reaction which causes effusion in the ordinary pleurisy should stop short at involvement of only one pleural sac. Again, why do many unilateral pleurisies occur in the absence of demonstrable pulmonary lesions, while gross pulmonary tuberculosis often runs its course without the development of pleural effusion? It seems obvious that we must presume a great complexity in the relationship between degree of allergy and dosage of tuberculotoxin and also a constant fluctuation in the state of this relationship. Of these factors, allergy would seem to be the more powerful. There is, no doubt, considerable scope in this field for further research.

CONCLUSIONS

1. A series of 45 cases of bilateral pleural effusions is presented. Tubercle bacilli were isolated from pleural fluid without guinea pig inoculation in 26.6 per cent of those aspirated, while bacilli were isolated sooner or later from some part of the body in 48.8 per cent of the whole series.

2. From a study of the above series it is believed that bilateral tuberculous pleural effusion is usually a manifestation of haematogenous dissemination and not infrequently of generalized miliary tuberculosis.

3. Bilateral pleural effusion has a distinctly graver prognosis than unilateral effusion. Active pulmonary tuberculosis follows more frequently; moreover, the subsequent appearance of disease in other organs is more common and typical miliary tuberculosis with multiple foci of disease, including lungs, may occur.

4. Because of the above, its importance as a harbinger of the appearance of disease in distant sites should be recognized.

5. Prognosis seems almost as bad with a considerable interval between effusions as when they occur simultaneously or close together.

6. Apparent absence of lung involvement at onset does not necessarily predict a more favorable prognosis and adequate treatment has less effect on end results than in unilateral effusion.

7. The pathogenesis of pleural effusion in general is discussed with special reference to that of bilateral effusion. The lack of any coherent theory of its pathogenesis shows the need for further research.

The author has prepared a master chart, listing all patients of the series reported and containing the pertinent clinical and pathological details. Copies of this master chart are available on request from the author.

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CLUBBED FINGERS IN PULMONARY TUBERCULOSIS[1]

RUBIN H. KAPLAN[2] AND LEONARD MUNSON[2]

Clubbed fingers and toes are a bulbous enlargement of the terminal phalanges producing a deformity resembling the end of a drumstick. Since the time of Hippocrates they have been considered a manifestation of chronic chest disease. Although their recognition was noted superficially no special diagnostic value had been associated with their presence and no adequate clinico-physiological explanation offered for their occurrence and incidence in certain diseases. It is only in more recent years, with the greater attention to minute details in the X-ray and clinical study of chest diseases and with the advent of chest surgery, that we again find their mention in the literature. This new emphasis is well exemplified in recent articles (1, 2) which state that primary clubbing of the fingers as a manifestation of or associated with hypertrophic pulmonary osteoarthropathy may constitute the initial complaint or sign in intrathoracic tumors. Clubbing has been noted to occur in cases of draining lung abscess and empyema, although closed abscess and empyema do not show its presence. Because of the increasing clinical interest, and having at our disposal a large group of cases of pulmonary tuberculosis, we have endeavored to determine the incidence, clinico-physiological significance and prognostic importance of clubbed fingers and toes in relation to phthisis.

Clubbed fingers and toes alone or associated with bony changes are generally conceded to be a manifestation of hypertrophic pulmonary osteoarthropathy. Most investigators (2, 3) have found that clubbing without periosteal changes is the more common finding in pulmonary tuberculosis. Clubbed fingers and toes are a bilateral, symmetrical, anteroposterior and lateral enlargement of the distal phalanges of the hands and feet. The nail, subcutaneous tissues and, in the more extreme cases, the periosteum are thickened, leading in time to the more charac-

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[2] Veterans Administration Facility, Castle Point, New York.

teristic convexity of the nail itself. Earliest findings are a bluish discoloration of the paronychium and contiguous tissue. This is followed by actual dusky cyanosis of the involved tissues. Campbell (4) secured a finger during life which manifested marked clubbing. Sections showed the enlargement to be primarily an oedema or engorgement of the soft tissues resulting in separation of the connective tissue fibres. Greatest thickening occurred between the bone and the nail bed. Periosteal changes in the fingers and less commonly in the long bones (2) may be found in more severe cases, but this generalized ossifying periostitis of the long bones is seldom associated with the clubbing initiated by pulmonary tuberculosis and its complications. The soft tissue changes are the primary and the earliest manifestations of hypertrophic pulmonary osteoarthropathy.

Clubbing of the fingers and toes is characteristically insidious and slow in onset and because of the lack of associated symptoms is seldom noted by the patient. Uncommonly, cases have been described in which the typical terminal phalangeal changes have occurred acutely and have progressed rapidly making their appearance in as short a period as two weeks (5). We have 2 cases in which an unusual rapidity was also noted. One had acute fulminating lobar involvement with a ten weeks' history of illness prior to admission, the patient dying approximately twelve weeks after onset. Clubbing of the fingers and toes was extreme. Another patient, with a history of pulmonary tuberculosis for five years and chronic bronchitis for fifteen years, developed typical clubbing under our observation during the terminal three months of his illness. Regression of soft tissue changes and even milder bony osteitis upon the improvement of the primary chest disease has been described (2, 3, 6).

The more important conditions other than pulmonary tuberculosis in which clubbing has been described are bronchiectasis, intrathoracic tumors, empyema, chronic pneumonia, chronic valvular and congenital heart disease, subacute bacterial endocarditis, Ayerza's disease, lung abscess and fungus infection of the lungs. Unilateral clubbing of the fingers has been described as secondary to aneurysm of the subclavian artery. Clubbing associated with extrapulmonary disease has not been substantiated.

Various theories (7) are postulated to explain the phenomenon. The aetiological factors described as most worthy of note are:

1: Toxaemia (8)
2: A peculiar type of amyloid disease

3: A manifestation of arthritic diathesis
4: A bony form of tuberculosis
5: A nerve disease resembling that associated with syringomyelia
6: Mechanical blood stasis
7: Toxaemia and circulatory stasis
8: Lack of oxygen
9: Predisposition of individual (9)
10: Peripheral changes secondary to right heart failure
11: Campbell's theory (4)

The latter theory, and the one which we feel most adequately explains the clubbing, is that a combination of decreased oxygen tension in the blood, associated with a slowing down of circulation, such as would occur in most dependent portions, produces the oedema and characteristic changes in the involved part.

Experimental studies (7) to reproduce clubbing in animals has been totally unsuccessful. These studies include:

1: The injection of bronchiectatic secretions and various organisms into rabbits.
2: Mechanical obstruction to produce venous congestion.
3: Ligation of bronchi in dogs.
4: Induction of intrathoracic complications in dogs, such as abscess, empyema, lobectomy and tuberculosis.

This report includes data on only such patients who were hospitalized at the time of our original classification on October 1, 1940. Patients with or without clubbing admitted to the hospital subsequently were not included. Sixteen cases were eliminated because of nontuberculous disease. Those originally included within the nonclubbed finger group who later developed this deformity, as has occurred in several cases, were not reclassified.

Various figures for the incidence of clubbing associated with pulmonary tuberculosis have been reported over a period of years. Locke (2) in 1915 lists an aggregate taken from various authors of 144 cases with clubbing in 30 cases, about 20 per cent. The Phipps Institute describes 772, or 21.7 per cent, of clubbing in 3,515 cases. Our series includes 426 male, tuberculous patients hospitalized at the Veterans Administration Facility, Castle Point, New York, of an average age of approximately forty-seven years. A total of 72 cases of varying degrees of clubbing, or 16.9 per cent, was noted. Of the total hospital census, 383 were white with 60 cases of clubbing, or 15.7 per cent, and 43 colored males with 12 cases of clubbing, or 27.9 per cent.

These figures, compared with the high incidence of clubbing in bronchiectasis, congenital heart disease, subacute bacterial endocarditis, etc., appear relatively low. The natural supposition, therefore, is that the clubbing is probably a sign or result, not of the initial pulmonary tuberculosis *per se* but of some complication, sequela, peculiar pathological type, degree of infection or intercurrent disease. We found no significant pulmonary complication in our series of cases to any greater degree or incidence than in our control group. Family history, general habitus, chest type, height, weight, span, finger-palm ratio, degree of cyanosis, history of haemoptysis, character and quantity of sputum, blood count and sedimentation rate, blood pressure, telangiectasia of the skin of the face and chest and dietary history showed no peculiar tendencies and were eliminated because of similar findings in the controls. Respiratory rate, vital capacity, mean temperature, pulse and dyspnoea were found

TABLE 1

	CASES	VENOUS PRESSURE	CIRCULATION TIME
		cm.	*seconds*
Clubbed finger group	22	10.6	6
Controls	11	10.2	6.2

essentially the same, except terminally. Venous pressures and circulation times were not done on terminal cases, and otherwise did not show any appreciable variations in the study of either group. (See table 1 (venous pressures were done by the direct method; circulation times by means of intravenous ether).)

The duration of the pulmonary tuberculosis, treatment, the age of onset, present age and surgical procedures, including pneumothorax, played no appreciably important rôle in our groups. The type, degree and extent of involvement were equally diversified, although in our clubbed group the tendency to progress more rapidly is undeniable. Despite the similarity in clinical findings, we feel that there must be an underlying pathological variation which predisposes the clubbed finger group to significant pulmonary vascular changes.

Attempts to ascertain the probable date of onset of clubbed fingers and toes and to correlate their occurrence with some significant factor in the course of the pulmonary disease failed. Unaccompanied by pain or discomfort and completely overshadowed by pulmonary and other symptoms, it is not surprising to note that these patients were entirely unaware of the deformity until it was quite obvious.

Clubbing of the toes occurred simultaneously in all our cases but 5, the latter having only minimal involvement of the fingers. Usually the degree of clubbing of the toes was less than that of the fingers. Involvement of the nose described in the literature as occasionally a part of the syndrome was encountered in only one of our cases. Objectively, we can say that clubbing usually occurs insidiously over a long period or may occur with comparative rapidity as in the 2 cases previously cited.

A majority of the patients with clubbed fingers and toes had more rapidly progressing pulmonary disease by clinical findings and X-ray interpretations. Serial X-ray films showed varying degrees of extension of the phthisic lesion since hospitalization.

TABLE 2

Status of clubbed finger cases over a four and one-half month period

	NUMBER OF CASES	PER CENT	COMBINED PER CENT
Improved	12	18.2	42.3
Stationary	16	24.2	
Progressive	14	21.2	57.7
Dying	9	13.6	
Died	15	22.8	
Totals	66	100	100
Unaccounted	7		

The clinical status of 66 cases was studied (7 of the total of 73 are unaccounted for, having left the hospital despite the advanced pulmonary disease); 38 patients, or 57.7 per cent, were classified as definitely progressive, dying or dead (see table 2).

As noted in table 2, 15, or 22.9 per cent, of our clubbed finger group died during the four and one-half month period of our observation. The total deaths among the remaining 353 patients was 26, or 7.3 per cent, during the identical period. Thus the mortality of tuberculous patients with clubbing is approximately three times that of patients not having this deformity. The difference in mortality rates must, therefore, be attributed to some factor present in the clubbed finger group and not encountered in the other.

The most definitely positive and significant clinical findings in our clubbed group were right heart changes. In 69 cases where the heart was examined, 64, or 93 per cent, exhibited positive findings; 37 cases, or

54 per cent, had a more pronounced or accentuated pulmonic second sound than the aortic; 8 cases, or 11.6 per cent, showed frank pulmonic localized murmurs; 58 cases, or 84 per cent, manifested variations in the tricuspid area, such as roughening, overt systolic murmurs or accentuated second sound. Frank systolic tricuspid murmurs were heard in 41, or 59.4 per cent, and were usually associated with these other right heart findings. The murmur, when present, was short in duration, moderately rough in character, of varying intensity and usually transmitted upward and to the left. Seventeen cases, or 24.6 per cent, showed only roughening of the first sound or accentuated tricuspid second sound.

In the control group of 61 cases, cardiac changes were elicited in 14, or 23 per cent. Of these, 3 had known old rheumatic lesions and one hypertensive heart disease. In only 5 cases, or 8 per cent, were the signs attributable to the right heart. (See table 3.)

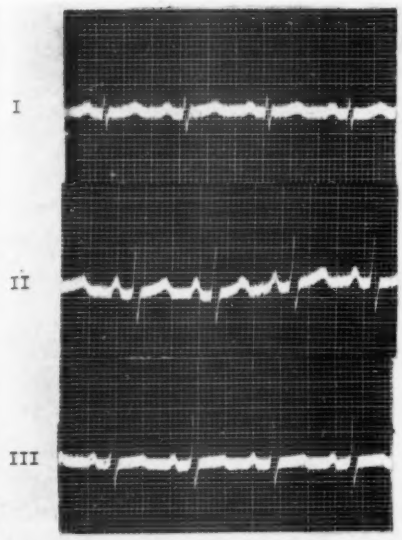
TABLE 3

	TOTAL CASES	HEART FINDINGS		RIGHT HEART FINDINGS		LEFT HEART FINDINGS		PULMONARY		TRICUSPID	
		Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Clubbed finger group.	69	64	93	64	93	5	7.2	37	54	58	84
Control group.....	61	14	23	5	8	9	14.8	2	3.3	4	6.5

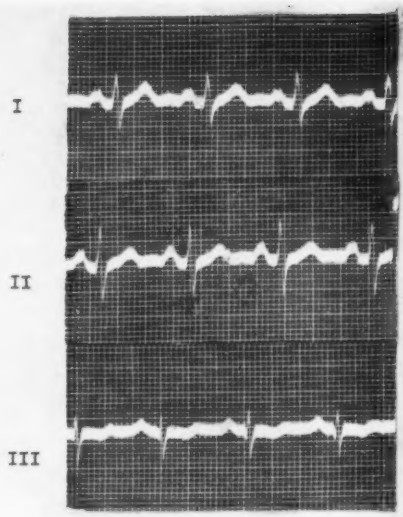
Electrocardiographic findings substantiate the right heart pathology. In 22 electrocardiograms of unselected nonhypertensive cases with varying degrees of clubbed fingers and toes, 7 cases showed right axis deviation and 2 more were equivocal but could be classed within this group, making 9, or 40.9 per cent; 2 cases, or 9 per cent, showed left axis deviation and the remaining 11 cases, or 50 per cent, had a normal axis.

P-wave abnormalities in more than one lead were noted in 9 cases, or 39 per cent of the entire group. The most characteristic and consistent observation was low voltage of the Q.R.S. complex and was seen in 20 of the 22 cases. Five cases of this group also showed similar low voltage in lead three. Incidental findings were not classified. The following electrocardiograms, leads I, II, III, were selected at random from the 22 in the clubbed finger group.

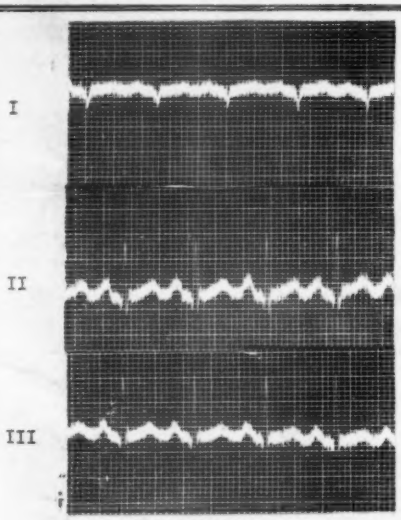
Leverton (10) analyzed the electrocardiographic findings in 416 cases of pulmonary tuberculosis, divided into a hypertensive and a nonhyper-



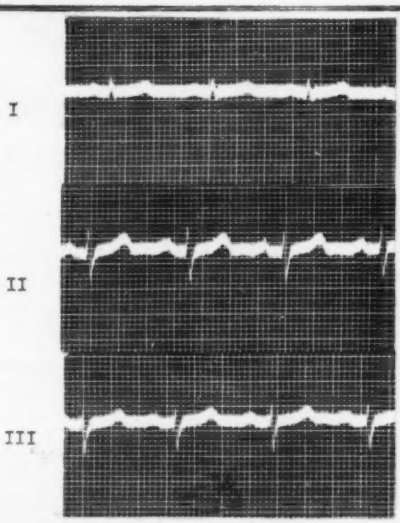
Low voltage I
Dicrotic "P" I
Right axis deviation



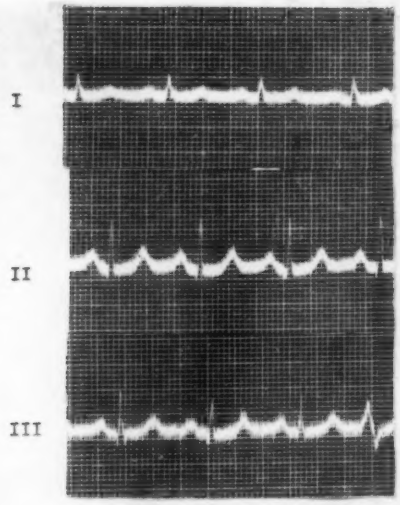
Low voltage I
Dicrotic "p" I & II
Abnormal "T" III
Questionable axis



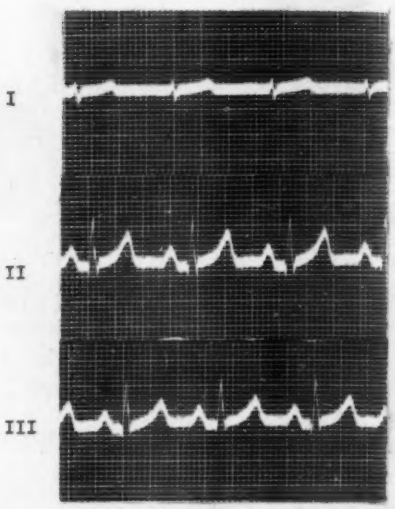
Low voltage I
Right axis deviation



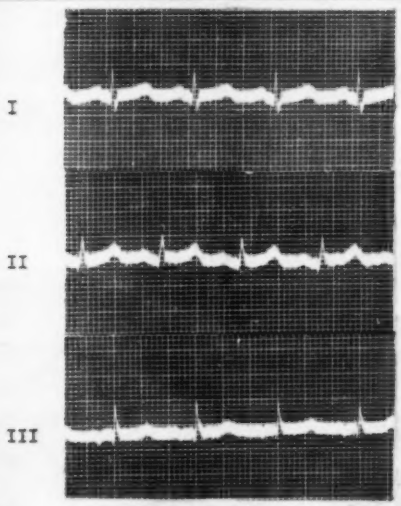
Low voltage I
Abnormal "P" in all three
Left axis deviation



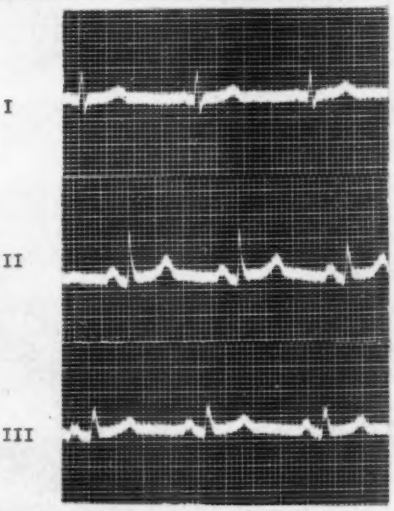
Low voltage I



Low voltage I
Right axis deviation
Absent "P" I



Low voltage all leads
Abnormal "P" I & III



Low voltage I & III
Abnormal "P" all leads

tensive group. A cross section of the results in his 378 nonhypertensive cases could be considered average electrocardiographic findings for tuberculous patients similar to ours, at a slightly younger age. His nonhypertensive group is otherwise completely unselected, no consideration being given to clubbing. He noted low voltage of the Q.R.S. complex in 24, or 6.3 per cent, right axis deviation in 63, or 16.6 per cent, left axis deviation in 28, or 7.5 per cent, and normal axis in 287, or 75.9 per cent. These findings are at a distinct variance with ours as noted in table 4. We must consider Leverton's findings in the light of the fact that the clubbed finger cases were included within his general group. We feel certain that if they were eliminated from his statistics our results would be at even greater variance.

TABLE 4

	TOTAL CASES	LOW VOLTAGE Q.R.S.	RIGHT AXIS DEVIATION	NORMAL AXIS	LEFT AXIS DEVIATION
		per cent	*per cent*	*per cent*	*per cent*
Nonhypertensive clubbed finger group	22	91	40.9	50	9.1
Nonhypertensive unselected tuberculosis (9)	378	6.3	16.6	75.9	7.5

DISCUSSION

The far greater mortality rate in our group must be accounted for by some pathological change not encountered in a similar group of cases of pulmonary tuberculosis without clubbed fingers. To produce such vital changes an important body organ or system probably is involved.

A review of our material focuses our attention on the significant cardiac findings limited for the most part to the right heart and corroborated by typical electrocardiographic changes which appear to be characteristic for this group.

Clinical interpretations of right sided heart sounds, such as are herein described occurring singly or in scattered cases, are only vaguely correlated with cardiac pathology. But findings occurring consistently throughout a large group of cases cannot be overlooked. Similarly, comparison of the aortic and pulmonary second sounds is at best equivocal, but in patients of this age group persistent accentuation of the pulmonary second sound is significant. The tricuspid valve (11) is the weakest of the four. Its leaflets barely meet in the normal heart. Any in-

crease in tension or dilation of the right ventricle, thickening of the muscle or strain on the chordae readily produce relative incompetency. These right heart findings probably indicate pulmonary hypertension, pulmonary arterial sclerosis, hypertrophy or dilation of the right ventricle or any combination of the four.

Actual physio-pathological basis for clubbed fingers must be theoretical at this time. However, we believe the most adequate explanation is that described by Campbell (4), in which he postulates that transfer of oxygen in the blood and tissues is dependent upon the relative oxygen tension. This is normally least effective in the most dependent portions of the body, such as fingers, toes and nose where circulation tends to be the slowest. A decrease in oxygen tension due to faulty aeration of the blood in the lungs regardless of the cause, plus a slowing of the circulation, leads to oedema. Most of our cases had cyanosis although in no appreciably greater degree than our control group. However, in spite of the fact that our circulation times were normal, the circulation in the dependent portions and capillaries was probably slower and less adequate than in the group where no abnormal right heart findings were noted. Since the primary pathology of clubbed fingers is oedema, we believe these cases to have a subclinical right heart failure. Thus demonstrating that, in this group where the oxygen tension is already lowered (7), an abnormal slowing down of peripheral circulation will in time lead to oedema and secondary clubbing of the fingers and toes.

Comparatively little has been written on the subject of pulmonary vascular pathology in chronic chest disease. Interest in the subject has been aroused in the past few years and various articles (12, 13, 14, 15) have been published describing some of these changes. Our knowledge of the sequence of events is less clear and less factual than is the description of the vascular variations occurring in the systemic circulation. Undoubtedly, pulmonary disease predisposes to pulmonary vascular changes, hypertension probably being the precursor of the sclerosis and then through strain of compensation producing *cor pulmonale*. This is similar to the hypertrophy of the left ventricle resulting from systemic hypertension and arteriosclerosis. We hope that the increasing interest will initiate further investigation with adequate postmortem material and that the studies will clarify and lead to a better understanding of these important physio-pathological phenomena.

Ackerman and Kasuga (12) in their description of chronic *cor pulmonale* stress the difficulty of antemortem clinical diagnosis. We believe that

the characteristic electrocardiographic change of low voltage Q.R.S. in lead I, associated with clinical right heart findings as previously described, and clubbing are pathognomonic even without decompensation. Although a definite statement cannot be made at this time because of our lack of postmortem material, the above authors in a series of 333 routine postmortem examinations on cases of pulmonary tuberculosis found an incidence of 16 per cent of *cor pulmonale*. This striking similarity to our clubbed finger incidence of 16.9 per cent indicates more than a casual relationship. It is unfortunate that they make no mention of the presence of clubbing in their review.

The results of our investigation prove that clubbing of the fingers is not the incidental clinically unimportant manifestation of chronic lung disease it is usually regarded but is of extreme importance in evaluating prognosis and surgical intervention. It indicates an embarrassment of the pulmonary circulation and of the right heart. Our mortality statistics in those with clubbed fingers as compared to those without shows an overwhelming increase in the involved group.

In view of these findings any surgical procedure should be looked upon with great trepidation and should be undertaken only after full evaluation of all clinical and prognostic data. Although intervention may temporarily alleviate the disease, the right heart and the pulmonary vascular system would probably be further embarrassed.

CONCLUSIONS

1. Clubbing of fingers has an incidence of 16.9 per cent in chronic pulmonary tuberculous patients of an average age of forty-seven years. The incidence in colored males is 27.9 per cent and in white 15.7 per cent.

2. Clubbed fingers associated with pulmonary tuberculosis indicate progressing pulmonary disease with a poor prognosis.

3. Clubbed fingers occurring in pulmonary tuberculosis are a manifestation of chronic *cor pulmonale* and are characteristically accompanied by clinical right heart findings and electrocardiographic variation of low voltage Q.R.S. complex in lead I.

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FOLLOW-UP OF 1,041 TUBERCULOUS PATIENTS[1]

MARGARET G. STEPHENS

This report of the experience of 1,041 tuberculous patients as regards rehabilitation and recurrence of their disease is divided into two parts:

I. What is the status of tuberculous patients on the third, fifth and tenth anniversaries of the date of admission to a sanatorium?
II. What are the chances that tuberculosis will recur after a patient has completed his cure and resumed employment?

The Metropolitan Life Insurance Company has a unique opportunity to answer these questions. It maintains at Mt. McGregor, New York, a sanatorium for its employees and agency force who are ill. Each year on the anniversary of discharge, a letter is written to each tuberculous ex-patient to ascertain the state of his health. Letters are sent both to those still in the service of the Company and to those who have left the service. The tracing has been successful: only 15 tuberculous ex-patients have been lost track of, but even they were traced successfully for a few years after discharge from the Sanatorium.

MATERIAL

This group of 1,041 tuberculous cases is drawn from two sources: "Home Office" at 1 Madison Avenue, New York City, and "Field" or sales force from the United States and Canada east of the Rocky Mountains. They were admitted to Mt. McGregor from 1919 through 1938 and have been followed through 1939. None had a history of previous cure for tuberculosis and they cured at Mt. McGregor for at least four months, except a few cases who completed their cure in less time. Cases which cured at Mt. McGregor for less than four months and then continued their cure under the care of their own doctor were omitted from this study since they represent cases which have not been as carefully supervised.

This study, then, shows the results obtained after curing under un-

[1] From the Medical Division, Metropolitan Life Insurance Company, New York, New York.

usually favorable circumstances. The patients may remain at Mt. McGregor until they are able to resume their duties. The cost of their care at Mt. McGregor is borne by the Company and in addition they receive weekly disability benefits under the Company's Group Health and Insurance program. When they are well, they are assured of resuming their employment in the Company under careful medical supervision.

The two sources, Home Office and Field, from which these patients came, differ in occupation, medical supervision and sex distribution.

The patients from the Home Office are composed of 92.7 per cent clerical workers and 7.3 per cent maintenance and commissary workers. Most of these patients are women (76 per cent). These people were under medical supervision before entering the Sanatorium and also after leaving the Sanatorium as long as they remained in the service of the Company. Since 1914 all applicants for employment have received preëmployment physical examinations and every employee has had an annual physical examination. From 1914 through 1924 detection of tuberculosis was dependent on signs or symptoms, in 1925 a roentgenograph was installed and used when indicated, and in 1928 a fluoroscopic examination of the thorax was added to the routine physical examination. Since 1928 the majority of the cases of tuberculosis have been detected by fluoroscopy before signs or symptoms were evident. As a result of this improved case-finding method, the proportion of cases detected in the minimal stage in this study has increased from 26 per cent in the period 1919–1925 to 62 per cent in the period 1934–1938.

The patients from the Field are agents (82 per cent) and women clerks (18 per cent) from the district offices. They too had preëmployment examinations and, after appointment to the Company, have been examined annually by qualified physicians in various cities where they work. Medical reports were reviewed at the Home Office where recommendations for further medical supervision were made when indicated. The detection of tuberculosis in this group was dependent chiefly on signs or symptoms. The proportion of minimal cases has not increased in the Field as it has in the Home Office since its use of fluoroscopy. Throughout the twenty-year period 1919–1938 about one quarter of the cases were detected in the minimal stage.

These two groups, then, differ in occupation and sex composition. They were under somewhat similar medical supervision except that the supervision at the Home Office since 1928 has included periodic fluoroscopy of the thorax and roentgenogram when indicated. They received

similar care during cure and when cure was completed they returned to their duties under medical supervision.

Table 1 gives the composition of the group, divided according to whether the patient came from the Field or from the Home Office and divided by sex, age and stage on admission.

TABLE 1

1,041 patients admitted to Mt. McGregor Sanatorium 1919–1938 for tuberculosis according to sex, stage and age

SEX, STAGE AND AGE AT ADMISSION TO MT. MCGREGOR	TOTAL	HOME OFFICE CASES	FIELD CASES
Total	1,041	492	549
Minimal			
Males	150	32	118
Age 17–24	15	12	3
Age 25–39	86	15	71
Age 40–64	49	5	44
Females	212	184	28
Age 17–24	137	122	15
Age 25–59	75	62	13
Moderately Advanced			
Males	280	63	217
Age 17–24	42	29	13
Age 25–39	142	20	122
Age 40–64	96	14	82
Females	197	151	46
Age 17–24	149	120	29
Age 25–59	48	31	17
Far Advanced			
Males	137	22	115
Age 17–24	20	10	10
Age 25–39	91	9	82
Age 40–64	26	3	23
Females	65	40	25
Age 17–24	49	35	14
Age 25–59	16	5	11

PART I

WHAT IS THE STATUS OF TUBERCULOUS PATIENTS ON THE THIRD, FIFTH AND TENTH ANNIVERSARIES OF THE DATE OF ADMISSION TO A SANATORIUM?

The answer to this question will help in planning tuberculosis programs, especially in industry, and may also be of service to individual patients.

The third, fifth and tenth anniversaries of admission to Mt. McGregor have arbitrarily been selected for study. The status on these anniversaries has been determined according to whether the persons were able to work, still curing, curing again or deceased. The material is presented by sex and stage at admission. Divisions by Home Office and Field, and by age are not presented here since it was found that those factors had no influence on the results.

From 1919 through 1936, 984 persons commenced their cure (table 2). On the third anniversary, 83.8 per cent of the males in the minimal stage were able to work as compared with 30.2 per cent in the far advanced

TABLE 2

Status on third anniversary of admission to Mt. McGregor Sanatorium. Admitted 1919 through 1936

M. L. I. Co. Home Office and Field

SEX AND STAGE ON ADMISSION	NUMBER OF CASES	PERCENTAGE				
		Able to work	Still curing	Curing again	Deceased	
					Tuberculous	Nontuberculous
Males						
Minimal	142	83.8	6.3	9.2	.7	—
Moderately advanced	271	57.6	25.1	8.8	6.6	1.9
Far advanced	129	30.2	38.8	4.6	26.4	—
Females						
Minimal	192	77.6	11.5	7.8	2.1	1.0
Moderately advanced	187	38.0	46.5	4.8	10.2	.5
Far advanced	63	12.7	49.2	1.6	36.5	—

stage; of the females 77.6 per cent in the minimal stage were able to work and 12.7 per cent in the far advanced stage. The percentage who had died increased with the extent of the disease on admission: 0.7 per cent of the males in the minimal stage and 26.4 per cent in the far advanced stage; 3.1 per cent of the females in the minimal stage and 36.5 per cent in the far advanced stage. The proportion of cases still curing on their third anniversary of admission increased with the increase of the extent of the disease.

Some difference was noted in the experience for the two sexes. The females in the moderately advanced and far advanced stages had a poorer experience than the males. In the minimal stage the differences were no greater than might be expected in chance sampling.

On the fifth anniversary (table 3) and on the tenth anniversary (table 4) the same results as regards stage hold true. The proportion of cases able to work was much greater among the minimal cases than among the

TABLE 3

Status on fifth anniversary of admission to Mt. McGregor Sanatorium. Admitted 1919 through 1934

M. L. I. Co. Home Office and Field

SEX AND STAGE ON ADMISSION	NUMBER OF CASES	PERCENTAGE				
		Able to work	Still curing	Curing again	Deceased	
					Tuberculous	Nontuberculous
Males						
Minimal	124	87.1	3.2	7.3	1.6	.8
Moderately advanced	246	62.2	11.4	12.2	11.8	2.4
Far advanced	121	32.2	19.9	13.2	33.9	.8
Females						
Minimal	159	86.2	3.1	6.3	3.8	.6
Moderately advanced	171	49.1	22.2	9.4	18.1	1.2
Far advanced	61	21.3	34.4	1.7	42.6	—

TABLE 4

Status on tenth anniversary of admission to Mt. McGregor Sanatorium. Admitted 1919 through 1929

M. L. I. Co. Home Office and Field

SEX AND STAGE ON ADMISSION	NUMBER OF CASES	PERCENTAGE				
		Able to work	Still curing	Curing again	Deceased	
					Tuberculous	Nontuberculous
Males						
Minimal	88	77.3	5.7	11.3	2.3	3.4
Moderately advanced	176	55.1	4.5	10.8	24.5	5.1
Far advanced	91	25.3	8.8	8.8	54.9	2.2
Females						
Minimal	81	86.4	1.2+	1.2+	9.9	1.2
Moderately advanced	115	47.8	6.1	7.8	35.7	2.6
Far advanced	51	29.4	9.8	3.9	56.9	—

moderately advanced cases. They in turn had a more favorable experience than the far advanced cases. Deaths from tuberculosis among persons who cured in the minimal stage were fairly infrequent even by

the tenth anniversary when over one-half of the far advanced cases had died.

On the fifth anniversary as compared with the third anniversary there was not as much difference between the findings for the men and for the women. On the tenth anniversary the results for each were about the same; the apparent differences are not statistically significant.

Conclusion: As measured by ability to work three, five and ten years after beginning to cure, the minimal cases had a much more favorable experience than the moderately advanced cases while the far advanced cases showed the poorest results. The proportion of cases who were curing on the specified anniversaries and those who had died increased with the greater extent of the disease.

For the first few years the males in the advanced stages had a more favorable record than the females but at the tenth anniversary there was no significant difference in the findings for the two sexes.

In this material, age at beginning of cure or source of the cases, that is, Home Office or Field, had no influence on the status at the specified anniversaries.

PART II

WHAT ARE THE CHANCES THAT TUBERCULOSIS WILL RECUR AFTER A PATIENT HAS COMPLETED HIS CURE AND RESUMED EMPLOYMENT?

This study is based on the follow-up records of 761 ex-patients who completed their cure and were able to return to employment prior to December 31, 1938. Their after-history has been traced to the 1939 anniversary of the completion of cure.

In this study "completion of cure" is defined as the time when the patient resumes his occupation. In most cases the disease was arrested or apparently arrested, but in any event the patient was considered able to resume his usual occupational duties. The majority (87 per cent of the minimal cases and 74 per cent of the advanced cases) completed their cure at Mt. McGregor. The others cured at Mt. McGregor for at least four months and completed their cure under the care of their own physician.

"Recurrence" is defined as reactivation of tuberculosis with resumption of cure. Many returned to Mt. McGregor to cure. Those who had left the service of the Company cured at other sanatoria or at home. "Recurrence rate" should not be confused with "readmission rate," since many who resume cure do not go to any sanatorium.

When calculating the recurrence rate it was essential to take into consideration the varying periods of follow-up. It would be quite misleading to tally the recurrences on the basis of the number of ex-patients regardless of whether they completed their cure one year ago or several years ago. Therefore a method was used whereby due allowance was made for the varying length of follow-up.

The recurrence rate was calculated by tallying the number of persons who had been followed at least one year, that is, those exposed to the risk of recurrence in the first year after completion of cure, and dividing it into the number who had a recurrence of tuberculosis that first year of follow-up. Thus, it made no difference whether a person cured in 1920 or 1930 or any other year. The important fact is that everyone in this group was exposed to the risk of recurrence for at least one year—hence the "recurrence rate" for the first year after completion of cure. The recurrence rate for the *second* year was obtained by taking the number of ex-patients who were traced to their *second* anniversary of completion of cure and who had stayed well during the first year. This number in the second year was divided into the number of recurrences in the second year; and so on.

A reproduction of the card used for keeping the data for each patient may be of interest. The card is read as follows:

Name	Case No.	Sex	At Admission: Stage	Age
Jones, John	141	M	M.A.	26
	District: H.Q. clerical			

Laboratory: Sputum positive	Guinea pig inoculation positive	Gastric washings positive	Pneumothorax	Phrenic nerve	Pneumolysis	Thoracoplasty	Length of Cure: Years	Months	Date Discharge

Sanatorium Residence	Years	Months	Follow-up			
3/26 to 7/27	1	4	12/28	✓		
Continued cure to 12/27		5	12/29	✓		
Date of death 7/33			12/30	✓		
Cause of death Pulm TB			12/31	✓		
			6/32 - 7/33	Mt MoG		

Anniversary 1 2 3 4 5 6 7 8 9 10

John Jones, of Home Office, clerical, began to cure in the moderately advanced stage at age twenty-six.

He cured at Mt. McGregor from March, 1926 to July, 1927, one year and four months.

He continued his cure under the care of his own doctor to December, 1927, an additional five months.

The length of his cure was one year nine months.

The date of discharge (or termination of cure) was December, 1927.

In December, 1928, his first anniversary of completion of cure, he replied to the follow-up letter sent to him from the Sanatorium stating he had been well and working during the year. A check (√) was entered on the card and at the bottom of the card a line was drawn to the first anniversary. This case is tallied as one case exposed to the risk of recurrence for one year after completion of cure.

On his second anniversary he stated he had been well during the year and had not cured. The line at the bottom of the card was continued to the second anniversary. The case is tallied as one traced to the second anniversary of completion of cure with no recurrence in the first year; and so on.

On the fifth anniversary we find that he had been readmitted to Mt. McGregor in June, 1932. A double broken line is drawn from June, 1932 to December, 1932. This case is counted as one exposed to the risk of recurrence in the fifth year after completion of cure and is also counted as a recurrence in that year. The case will be dropped from further calculation of the rate of recurrence, but follow-up will be continued for additional information.

On the sixth anniversary it is noted that he continued to cure until July, 1933 when he died of pulmonary tuberculosis. The double broken line was carried to July, 1933 and the case was closed. Date and cause of death were entered in the appropriate spaces.

A glance at the card will give information as to his status on any date desired. The back of the card has space for follow-up to the twentieth anniversary of completion of cure.

Table 5 presents the recurrence rate by sex and stage for each of the first ten years of follow-up and also shows the average recurrence rate per year in the first five-year period and in the second five-year period. In the first five years after completion of cure for minimal tuberculosis, 139 males were exposed 532 years to the risk of recurrence of their tuberculosis; 139 were exposed the first year, 13 had a recurrence and 7 had completed their cure only one year previously so could not be counted in the exposure for the second year. The rest, or 119, were exposed in the second year (equivalent to 119 exposure-years); 10 had a recurrence and five had completed their cure only two years previous to the end of the follow-up in 1939, leaving 104 exposed in the third year; and so on.

For the males in the minimal stage the rate of recurrence seems to decline after the third year; however, the apparent decline in the fourth

and fifth years is not statistically significant and may be due to chance fluctuation.[2]

The rate of recurrence for males who cured in the minimal stage averaged 7.3 per cent per year for five years. This is equivalent to saying

TABLE 5

Recurrence of pulmonary tuberculosis according to time elapsed since completion of cure

Began cure 1919–1938; completed cure prior to 12/31/38. Traced to 1939 anniversary of completion of cure

Home Office and Field ex-patients

PERIOD SUBSEQUENT TO COMPLETION OF CURE	NUMBER OF YEARS-OF-LIFE EXPOSED TO RISK OF FIRST RECURRENCE				PERCENTAGE OF RECURRENCES PER YEAR			
	Males		Females		Males		Females	
	Minimal	Advanced	Minimal	Advanced	Minimal	Advanced	Minimal	Advanced
First 5-year period.....	532	974	762	618	7.3	11.2	3.9	6.1
Second 5-year period...	287	381	362	242	1.7	2.6	2.8	1.6
1st year.....	139	275	187	160	9.4	13.1	2.7	6.9
2nd year.....	119	228	172	142	8.4	11.0	7.6	7.7
3rd year.....	104	192	150	124	9.6	10.9	3.3	7.3
4th year.....	88	155	132	104	3.4	12.3	1.5	1.0
5th year.....	82	124	121	88	3.7	6.5	4.1	6.8
6th year.....	76	106	102	74	2.6	5.7	4.9	4.1
7th year.....	65	86	88	60	3.1	—	3.4	—
8th year.....	55	73	72	48	—	1.4	1.4	—
9th year.....	49	64	57	37	2.0	—	1.8	2.7
10th year.....	42	52	43	23	—	5.8	—	—

that 36.5 per cent of this group will have had a recurrence when they all have attained their fifth anniversary of completion of cure.

[2] Throughout this study the formula used to test for statistical significance was:

$$\sigma = \sqrt{\frac{p \times q}{n} + \frac{p' \times q'}{n'}}$$

Where σ = the standard error of the difference $(p - p')$
p = per cent of non-recurrences in a specified group
q = per cent of recurrences (100 per cent $- p$)
n = number in a specified group
p' = per cent of non-recurrences in contrasting group
q' = 100 per cent $- p'$
n' = number in contrasting group

When difference in the percentages of the two groups $(p - p')$ is more than twice the standard error, the difference is considered significant.

The females who cured in the minimal stage showed fluctuations in the recurrence rate from year to year. They had an average recurrence rate of 3.9 per cent per year, equivalent to 19.5 per cent of the group in a five-year period.

The males in the advanced stages (moderately and far advanced) had an average recurrence rate of 11.2 per cent per year or 56.0 per cent in five years as compared with females in the advanced stages who had an average of 6.1 per cent per year of 30.5 per cent in five years.

These figures are, of course, high compared with readmission rates but readmission rates tell only part of the story.

TABLE 6

Status on fifth anniversary of completion of cure

Cases which completed cure and were ready to work prior to 12/31/34

Admitted 1919–1934

STATUS ON FIFTH ANNIVERSARY OF COMPLETION OF CURE	MINIMAL				ADVANCED			
	Males		Females		Males		Females	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Total	117	100.0	135	100.0	225	100.0	114	100.0
Able to work	104	88.9	122	90.4	168	74.7	87	76.3
Have worked continuously	81	69.2	107	79.3	118	52.5	79	69.3
Have cured again	23	19.7	15	11.1	50	22.2	8	7.0
Curing again	10	8.5	10	7.4	42	18.7	16	14.0
Dead								
Tuberculosis	2	1.7	2	1.5	9	4.0	9	7.9
Not tuberculosis	1	.9	1	.7	6	2.6	2	1.8

Another presentation of this material on recurrences is of interest; that is, the status of these ex-patients on the fifth anniversary of *completion* of cure. Cases who completed their cure prior to December 31, 1934 are cited because all of these could be observed on the fifth anniversary of returning to work. The experience is shown in table 6.

This table is of special interest because it aids in predicting the outcome of completed cure. Of those who cured in the minimal stage, about 90 per cent were at work (or able to work) on their fifth anniversary of completion of cure. Four had died of tuberculosis. Within that period, 19.7 per cent of the men and 11.1 per cent of the women had completed a second cure; this apparent difference is not statistically significant.

The experience of those who had cured in the advanced stages was

less satisfactory. About three-quarters were able to work on their fifth anniversary of completion of cure. Eighteen had died of tuberculosis. In that period 22.2 per cent of the men and 7.0 per cent of women had cured a second time. The second cure was of shorter duration for the men than for the women. In spite of the greater proportion of recurrences among the men, their status on the fifth anniversary was comparable to that of the women.

All of the material has been studied (but not shown here in detail) according to date of admission, duration of cure, age at admission and source of material, that is, from Home Office or Field. It was found that the recurrence rate was not influenced by any of these factors except possibly date of admission. There is some indication that those who went to Mt. McGregor in the early 1920's had a higher recurrence rate than those who went in the 1930's. No satisfactory explanation can be offered.

Another inexplicable finding is the similarity of the experience of the Home Office and Field cases. As noted above, the cases have been discovered early in their disease by fluoroscopy at the Home Office since 1928. We know that the Field cases have not increased their proportion of minimal cases as has the Home Office. But it was supposed that the minimal cases detected early in their disease and the advanced cases detected early would show a more favorable record than the Field cases which were detected only by physical signs or symptoms. Of course it should be remembered that some of the groups are quite small. As the amount of material increases we shall watch the comparison with interest. Fluoroscopy has detected the majority of the cases in the minimal stage. This method of case-finding is of great value: the data definitely indicate that the minimal cases have an advantage over the advanced cases from every point of view.

Conclusion: The cases which were admitted to Mt. McGregor in the minimal stage had fewer recurrences of their tuberculosis after they returned to work than those admitted in the advanced stages.

The females had fewer recurrences than the males.

In a five-year period after completion of cure in the minimal stage, about one-third of the men and one-fifth of the women cured again; and in the advanced stages over one-half of the men and almost one-third of the women cured again. This was experienced in spite of favorable conditions during the first cure and supervised rehabilitation.

On the fifth anniversary of *completion* of cure 90 per cent of the minimal

cases were at work or able to work as compared with 75 per cent of the advanced cases.

COMMENT

Detection of tuberculosis in the minimal stage is admittedly of great advantage from every point of view. This study furnishes a yardstick to measure the actual difference in the experience for the minimal and for the advanced cases.

It is interesting to note the proportion of cases whose cure was terminated by death. Experience of the admissions of 1919 to 1933 was selected since 95 per cent of these cases have terminated their cure. Cure was terminated by death in 1.5 per cent of the minimal cases, 20.7 per cent of the moderately advanced cases, and 46.9 per cent of the far advanced cases.

Another finding of interest in this material concerns the duration of cure. The minimal cases cured a shorter time than the advanced cases. Of 414 minimal cases who resumed work, about three-quarters had cured one year or less. Of 435 advanced cases who resumed work, less than one-third had cured one year or less; about one-third cured three years or more.

SUMMARY

Follow-up data on 1,041 tuberculous patients from the Metropolitan Life Insurance Company have been presented.

The study has been divided in two parts:

Part I What is the status of tuberculous patients on the third, fifth, and tenth anniversaries of the date of admission to a sanatorium?

Part II What are the chances that tuberculosis will recur after a patient has completed his cure and resumed employment?

The source of the material and the technique of the study have been described in detail.

Acknowledgment: The careful follow-up and tracing of the ex-patients has been done by Miss Wesleyna Smith of the statistical office, Mt. McGregor Sanatorium.

CASE-FINDING IN THE CHINESE POPULATION OF SAN FRANCISCO[1, 2]

WILLIAM C. VOORSANGER[3] AND GEORGE B. MILLER

"I wish to remark
And my language is plain
That for ways that are dark
And for tricks that are vain
The heathen Chinee is peculiar
Which the same I would
Rise to explain." (BRET HARTE)

And that is why it took us thirty years to make a survey of tuberculosis in the Chinese section of the city of San Francisco. The first examination was scheduled for April 19, 1940, at St. Mary's Mission, one of the social and health centres of Chinatown. The arrangements for this initial meeting had to be carefully planned by the social workers, nurses, both Chinese and white, and physicians who were competent fluoroscopists. Naturally we approached this zero hour with a feeling of trepidation, having failed so often to get coöperation from the Chinese population. We were therefore astounded when several hundred Chinese presented themselves at eight p.m. for this fluoroscopic examination. From the opening night the work proceeded uninterruptedly until to-day we have examined roentgenologically over 2,000 Chinese, out of a supposed total population of 17,000. We say "supposed," because we have never felt in San Francisco that the census could ever be one hundred per cent correct on our Chinese population. Before giving the results of this survey it will be of great interest to you to know a little of the struggles over a period of more than thirty years, during which time neither the San Francisco Tuberculosis Association nor the San Francisco Department of Public Health ever relaxed their efforts to ascertain accurately the amount of actual tuberculosis in the Chinese population.

[1] Read before the annual meeting of the California Tuberculosis Association at Del Monte, California, April 4, 1941.

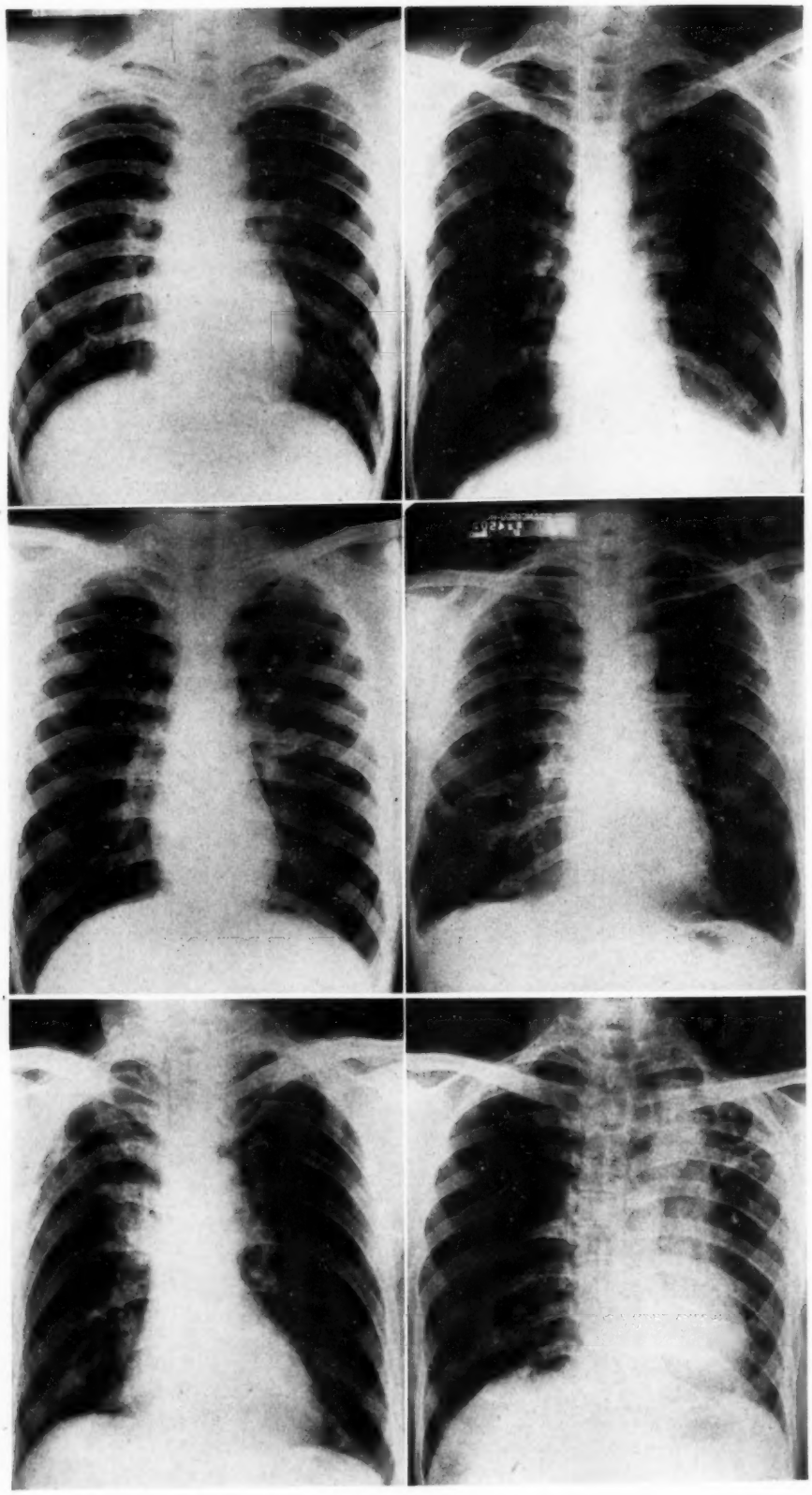
[2] Under the auspices of the San Francisco Tuberculosis Association. Committee: Drs. Sidney Shipman, George H. Becker, Carl F. Meyer, William C. Voorsanger, Father Richard T. Howley and the San Francisco Department of Public Health, Dr. J. C. Geiger, Director.

[3] 490 Post Street, San Francisco, California.

When the San Francisco Tuberculosis Association was organized in 1908, the first piece of work in which it engaged was the making of a spot map of the city and county. This shows the wide spread of tuberculosis in the city at that time; it shows a very black section, known as our Chinese and North Beach section. It was plain to us at this time that it must be our chief endeavor to control tuberculosis among the Chinese population, if we were ever to get a low death rate from tuberculosis in the city as a whole. In the years from 1908 to 1910, the death rate per 100,000 for the Chinese was given as 510.3. The death rate for the city as a whole was something under 300. In 1919 the death rate in the Chinese population had reached to over 800. For 1939 the death rate for the Chinese population dropped to 205, as against a city-wide death rate of 64. One might think from this that the Chinese death rate has fallen in the same proportion as the white death rate. However, when we consider that the national death rate from tuberculosis for the year 1940 will probably be 45 or under, the San Francisco death rate is entirely too high, and we naturally feel that it is due to the high Chinese death rate. The minutes of the Tuberculosis Association for the years from 1910 to 1940 constantly contained recommendations such as this under the date of May 11, 1910: "After discussion it was moved and seconded that if the Six Companies shall assume all of the financial burden of the establishment and the operation of a clinic, that the Association will gladly assist in providing the medical supervision and the direction of the sociological features. Carried." Through the years we find notes constantly of literature which had been translated from English into Chinese on phases of tuberculosis prevention. We note under the date of September 20, 1916 that Mr. Wong, Secretary of the Chinese Six Companies, and Mr. S. G. Shu, Chinese Consul General, were in conference with the Secretary of the Tuberculosis Association relative to the engaging of a Chinese nurse. The first Chinese Clinic was opened in January, 1918, at 40 Trenton Place. In 1920, 122 adults and 103 children were handled by the Chinese Clinic. When the Chinese Hospital was established an attempt was made by several of us to put in a tuberculosis clinic. As late as November 19, 1929, we find a note, "The question of undertaking additional work in Chinatown, either by opening a tuberculosis clinic at the Chinese Hospital, or by employing a Chinese woman to work under the direction of the Board of Health nurse in that district in stimulating Chinese attendance at the already established tuberculosis clinics, was discussed." I remember several meetings with the

late Doctor Hassler, then Health Officer for the City and County of San Francisco, and his almost fanatical desire to do something to control tuberculosis in the Chinese section. He repeatedly stated that his efforts seemed always to end in a blind alley. The Health Department felt that the Chinese Six Companies did not wish to see a Chinese Tuberculosis centre established in Chinatown, due principally to the immigration laws, which excluded certain types of Chinese, and if such were illegally in the country and attended a clinic, complications might ensue. In spite of our assurances at all times that we were not interested in immigration laws but in the control of tuberculosis, the impasse continued.

Perhaps another reason can be given for the long years we have had to wait to make this survey. A Chinese cannot be commanded or frightened. He must be either convinced or coaxed. When one has lived all his life in this City, with a Chinese population we believe to be the largest of any city in the world outside of China, which is estimated to-day at approximately 17,000 and which at one time was perhaps even greater, packed into a very small area (about twenty square blocks), he realizes that we are dealing with an alien population of very considerable size with fixed ideas on medicine, health and education. Bret Harte is quite correct in regard to the older Chinese population when he says the Chinese is "peculiar." I also feel that I am right, that the Chinese must be convinced. So we finally convinced him, principally because during the past thirty years a new generation of young Chinese, born and educated in the city of San Francisco, has grown up, and although we were surprised at the wonderful reception with which this survey met for the first time during our endeavors, the enthusiasm is explainable. We feel that this work is epoch making. To my knowledge, no report of a mass survey of a Chinese population has ever been made, even in China. This survey was organized by a committee of the San Francisco Tuberculosis Association and the San Francisco Health Department (see title page). This committee, with the assistance of Mr. Paul Neiman, Secretary of the San Francisco Tuberculosis Association, prepared the way carefully by getting all the Chinese social, religious and health centres coöperating. The opening examination, as stated previously, took place at the Chinese Catholic Centre commonly referred to as "St. Mary's." Then at intervals of from two to three times a week, meetings and examinations were held at the Chinese Young Men's Christian Association, the Chinese Young Women's Christian Association, the Chinese Baptist Church, the Chinese Presbyterian and Methodist Episcopal Churches. All the



FIGS. 1–6

Chinese doctors, some twelve in number, and executives of social organizations coöperated to the fullest. The fluoroscopic work was performed by Drs. George B. Miller, Angelina Piscitelli, Fred C. Blake, Milton Seid, Otto Hatschek and I. Clinton. The evaluation of the medical end of the work was principally in the hands of Dr. George B. Miller.

After the initial arrangements were made, they had to be executed with a little more care than is usually necessary in making a survey in other large groups, such as Negro or Mexican. A Chinese nurse was employed for follow-up work among the Chinese. A Chinese interpreter was also engaged. Pamphlets of information were printed in English and Chinese, as were cards pertaining to examination dates. This work could never have been successfully accomplished without the coöperation of all parties concerned, particularly the San Francisco Health Department and the Health Centre in Chinatown, in charge of a Health Department nurse, Miss Eunice Gibson. Most of these sessions were held from seven until ten o'clock at night. Usually three or four physicians were occupied in the program, so that no doctor was at the fluoroscope continuously for more than one hour. Reports were dictated to a nurse and, where tuberculosis was suspected, a 14 x 17″ film was recommended. If the fluoroscope revealed any suspicion of tuberculosis, the patient was referred either to a private physician or, as in most cases, to the chest clinic of the San Francisco Hospital. We had already received assurance from the City Health Department that we could hospitalize all active cases of tuberculosis. The number of cases discovered among the 2,000 examined was 54. Figures 1 to 6 show some X-ray pictures taken of cases which were discovered by the fluoroscope. The scope of this paper will not permit going into all the

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FIG. 1. (Upper left.) Age thirty-seven years. Minimal active tuberculosis, demonstrating early active type of case picked up.

FIG. 2. (Upper right.) Age twenty-five years. Early active case of tuberculosis which went on to death, demonstrating the significance of picking up early lesions and at least isolating them.

FIG. 3. (Center left.) Age seventeen years. Early active case of tuberculosis picked up at ideal time to start treatment.

FIG. 4. (Center right.) Age fifty years. Minimal apparently inactive tuberculosis. This type of case is held under observation in the Out-Patient Department.

FIG. 5. (Lower left.) Age sixty-three years. Healed moderately advanced tuberculosis seen with unexpected frequency in routine roentgen surveys among the Chinese population.

FIG. 6. (Lower right.) Age thirty-seven years. Far advanced case proven inactive clinically. Patient did not know he had ever had a serious ailment and arrestment was spontaneous.

fascinating details of the human side of this survey. We are going to try to present facts and results. First, our survey has shown a greater incidence of active tuberculosis in the Chinese population of San Francisco than in the white. Much excellent work has been done by the San Francisco Health Department in discovering tuberculosis in Chinatown, but the intensive work done under this survey discovered many cases not known previously. In July, 1940 there were registered 1,343 Chinese with tuberculosis out of a total of 7,138 for all of San Francisco, or 19 per cent of the total, although the Chinese population is only 2.75 per cent of the total. See table 1.

TABLE 1

	ADULT	10-21	0-10	TOTAL
Tuberculosis cases registered with Department of Public Health, July, 1940				
All San Francisco	1,919	641	279	2,839
Chinese	215—11%	220—34%	94—34%	529—19%
Contacts supervised by Health Department				
All San Francisco	3,802	1,990	1,346	7,138
Chinese	533—14%	541—27%	269—20%	1,343—19%

This incidence, with intensive survey and follow-up, will prove to be even larger. Intensive public health work in the Chinese has been followed by marked reduction in the tuberculosis death rate. It is, however, more than four times that of the rest of the population. See tables 2 and 3.

A curve of the death rate in San Francisco from the years 1908 to 1940 contrasted with the national death rate demonstrates this point very clearly (see chart 1). The rates from which this chart was drawn are based upon Chinese deaths from tuberculosis as recorded by the San Francisco Department of Public Health and the Chinese population as recorded by the Federal Bureau of the Census. Note that in 1917 about one out of every hundred Chinese in the city died of tuberculosis. In that year there were 84 deaths from tuberculosis among the 8,600 Chinese then in San Francisco. It is probable that the Chinese population of San Francisco in earlier years was larger than indicated by the census. Tables 4, 5 and 6 show the number of cases fluoroscoped and the kind of tuberculosis detected subsequently on 14 x 17″ films.

TABLE 2

Tuberculosis death rates—1940

San Francisco Chinese	268
All others in San Francisco	60
United States	46

TABLE 3

	NUMBER	PER CENT
Population of San Francisco—1940		
Chinese	17,500	2.75
All other	616,900	97.25
Total	634,400	100
Tuberculosis deaths in City—1940		
Chinese	47	11.2
All other	373	88.8
Total	420	100

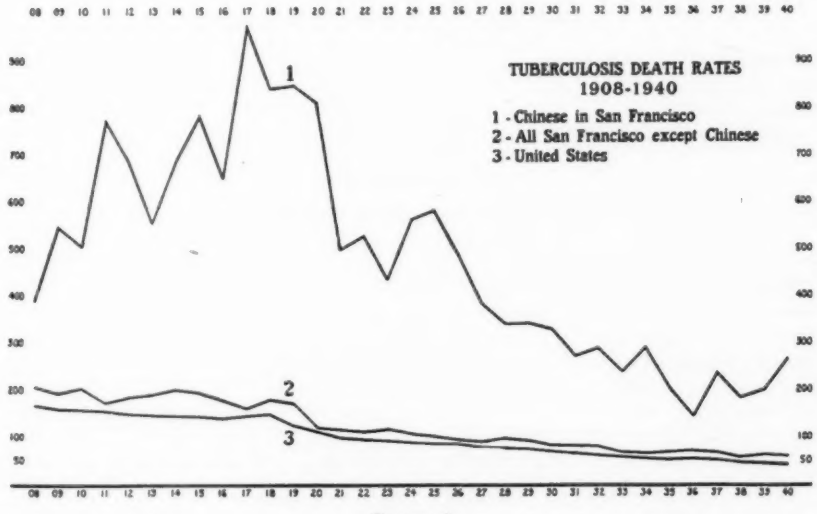

CHART 1

Table 7 shows a classification of 26 cases who have not yet reported for X-ray pictures. We feel, however, since there has been a very small percentage of error in our fluoroscopic findings that probably in 80 per cent of these cases the original diagnosis will not be changed by the films.

Table 8 gives the disposition of these cases, and it should be noted that no survey can prove of value unless proper disposition is made of the newly discovered cases. In this regard we have had no trouble whatever, since our Health Department has coöperated to the fullest in disposing satisfactorily of all patients who could not afford private care.

TABLE 4

Fluoroscopic examinations in Chinese district

Chinese examined	1,958
Negative on fluoroscopy	1,878
X-ray films recommended for	80
No report yet	26

TABLE 5

Diagnosis of 54 X-rayed

Active tuberculosis	16
Apparently healed tuberculosis	27
Nontuberculous, or minimal, obsolete tuberculosis of no clinical importance	11

TABLE 6

Diagnosis of 27 apparently healed cases

Far advanced	1
Moderately advanced	3
Minimal	23

TABLE 7

Classification of 26 not yet X-rayed

(Classified by fluoroscopy alone)

Probably active-advanced	2
Probably active-moderately advanced	2
Probably healed-minimal	3
Probably tuberculous-activity unknown	5
Insufficient evidence for classification by fluoroscopy alone	14

Table 9 shows the percentages by age and sex.

Male, 1,561—79.7%. Female, 397—20.3%.

We note from this table that 41.31 per cent of all cases are in the 15–29 age group. This does not differ from the rest of the population; 80 per cent of the total examined were more than twenty years of age. We eliminated the young people of school age in the Chinese community because they have been tuberculin tested previously by the Health

Department. There were, however, a considerable number of Chinese of school age fluoroscoped who had recently arrived from China.

Table 10 shows the difficulty of follow-up work in a Chinese population, where so many have the same name. It can readily be understood that

TABLE 8

Medical supervision for 54 examined with X-ray films

Active Tuberculosis		16
Hospitalized	8	
Health Department clinic supervision	5	
Private M.D. supervision	3	
Apparently Healed Tuberculosis		27
Health Department clinic supervision	25	
Private M.D. supervision	2	
Nontuberculous or minimal, obsolete tuberculosis of no clinical importance. No medical supervision needed		11

TABLE 9

1,958 Chinese by age and sex

		per cent
Under 15	72	3.67
15–19	317	16.19
20–29	492	25.12
30–39	428	21.85
40–49	364	18.59
50–59	159	8.12
60–69	94	4.80
Over 70	29	1.48
Age not given	3	0.15

TABLE 10

Common Chinese family names among 1,958 records

Lee	221	Louie	55
Wong	218	Leong	54
Fong	77	Tom	53
Chan	66	Chin	47
Yee	65	Ng	40

to find the right Mr. Lee or the right Mr. Wong in a large rooming house was a difficult task. Our procedure to overcome this was to hire a Chinese clerk to register applicants, and to have the Chinese nurse stand beside the doctor. She then led away immediately and made clinic

appointments at once for those whom the doctors chose for further examination. After this procedure was put into effect subsequent examination with X-ray films was obtained on virtually all suspected cases.

Studies of the X-ray pictures demonstrate a large number of apparently healed lesions. There should not be too much significance attached to finding this large percentage of apparently healed lesions. We know that tuberculosis has been rampant and uncontrolled in the Chinese population for years, and many cases of tuberculosis have doubtless healed spontaneously, or under some kind of medical care. We should like to flirt with the idea of immunity or resistance in the Chinese on the assumption that, although a large community has lived under poor conditions for many years, with tuberculosis uncontrolled, a certain amount of healing has taken place, which perhaps indicates rather a high resistance to tuberculosis in the Chinese, contrary to the belief that their resistance to the disease is low. This, of course, is purely theoretical at the present time, but a study of this theory might produce some definite facts. At the time this survey was going on, 2,000 white adults from the San Francisco State College were fluoroscoped. The incidence of tuberculosis in this white group was 0.1 per cent. This of course was a select group. The incidence in the Chinese population was approximately 54 in 2,000, or about twenty times as many as in the white group. This comparison perhaps should not be made, since the State College group comes from a more sanitary environment than the Chinese group, and they represent a different age distribution. The age distribution of 47 Chinese diagnosed as having clinically significant tuberculosis is as follows:

Age Group	*Number*
10–19	8
20–29	8
30–39	8
40–49	13
50–59	3
60 and over	7
Total	47

The Chinese were the first to invent the expression, "One should first look, and then one should look-see." For thirty years we have looked. We believe that, with the improvement in our fluoroscopic methods and the ability of the physicians employed to interpret the findings, we now "look-see."

CONCLUSIONS

1. The possibility of an intensive tuberculosis survey in a large Chinese population has been demonstrated for the first time.

2. The incidence of tuberculosis in the San Francisco Chinese population is 19 per cent of the total tuberculosis incidence, although the Chinese population is 2.75 per cent of the total population.

3. All active cases of tuberculosis were either hospitalized or placed under proper supervision.

4. Careful fluoroscopy by experienced fluoroscopists, followed by 14 x 17″ films in suspicious cases, is an effective means of discovering tuberculosis.

5. The large number of persons with apparently healed tuberculosis and with calcifications demonstrates that the Chinese population through the years has taken care of its tuberculosis spontaneously and may change our view that their resistance to tuberculosis is low.

6. The work on the Chinese population will be continued. All cases discovered will be carefully followed and, as a result, we may be able to reduce materially the excessive death rate in the Chinese population.

CONCLUSIONES

1. Por primera vez se ha demostrado en este estudio la posibilidad de realizar un censo tuberculoso intenso en un numeroso grupo chino.

2. El coeficiente de tuberculosis entre los chinos de la ciudad de San Francisco representa 19 por ciento del coeficiente total para la población, aunque la población china sólo constituye 2.75 por ciento de la población total.

3. Todos los casos de tuberculosis activa fueron bien hospitalizados o colocados bajo vigilancia adecuada.

4. La roentgenoscopia cuidadosamente ejecutada por roentgenoscopistas avezados, seguida de la obtención de películas de 35 x 42.5 cm. en los casos sospechosos, constituye un medio eficaz para descubrir la tuberculosis.

5. El elevado grupo de personas encontradas con tuberculosis aparentemente cicatrizada y con calcificaciones, demuestra que la población china a través de los años ha atendido espontáneamente a su tuberculosis, y puede alterar nuestra opinión de que esa raza posee poca resistencia a la tuberculosis.

6. Estos estudios de la población china van a continuar. Todos los casos descubiertos serán seguidos cuidadosamente, y debido a ello tal vez podamos aminorar decididamente la excesiva mortalidad de los chinos.

PNEUMOPERITONEUM IN THE TREATMENT OF PULMONARY TUBERCULOSIS[1]

W. O. FOWLER[2]

Therapeutic pneumoperitoneum is relatively new and its value is still the subject of discussion. Many workers feel that is has nothing to offer and that bed-rest alone will do as much. Another group feels that it is invaluable and that it should be used on all patients who cannot qualify clinically and pathologically for a more direct form of collapse therapy. I feel that there is a middle ground between these two extremes which places pneumoperitoneum on a firm foundation, thus properly classifying it as a valuable and often indispensable addition to the surgical treatment of pulmonary tuberculosis. The true value appears to lie in its ability to improve the patient's general condition and alter the course of the pathological process, as demonstrated by X-ray, in such a manner that a more direct approach by radical surgical measures becomes safe. In many cases an adequate arrest of the disease can be obtained through pneumoperitoneum alone, thus justifying its existence; however, its value can be enhanced manifold by changing the mode of attack, when the peak of improvement has been reached, to the appropriate type of radical surgery. These statements will be enlarged upon in the statistical study and presentation of cases to follow.

The subject is so large for the time alloted that an adequate coverage of the literature becomes impossible. For that reason, I refer those who are interested to the bibliography for a consideration of the literature which forms the background of this study.

Overholt's work on dogs, Banyai's work on the far advanced cases of tuberculosis and numerous pathological reports from the literature on autopsy material adequately establish the safety of pneumoperitoneum from a pathological point of view. Trimble *et al.* report cases studied at autopsy and no constant changes in the abdominal viscera attributable to the air in the peritoneal space were found. We have had the privilege

[1] Presented before the Medical Section at the 37th annual meeting of the National Tuberculosis Association, San Antonio, Texas, May 7, 1941.

[2] State Tuberculosis Sanatorium, Orlando, Florida.

of studying 6 cases on the autopsy table and the only finding, grossly or microscopically, was a low grade irritation of the peritoneum. No deleterious effect on the abdominal viscera was noted. Five cases in the series being reported have had a laparotomy performed for intraäbdominal lesions and 4 of these have had the pneumoperitoneum continued, the fifth being lost because a peritoneal effusion developed. In none of these cases was it possible to demonstrate gross pathological changes attributable to the effect of air in the peritoneal space.

The following complications must be considered:

1. *Peritoneal effusion:* The incidence is quite low, 3.8 per cent in our series, and the deleterious effects are more dependent on the underlying lesions than on the effusion itself.

2. *Peritonitis:* We have not encountered this complication and I have been unable to find any figures to indicate its incidence.

3. *Ruptured viscus from instrumentation:* No cases have so far been reported and this complication can be avoided if a careful, adequate technique is adopted and rigidly adhered to.

4. *Ruptured diaphragm:* We have not encountered this complication but a few reports are now appearing in the literature. The incidence of this complication can also be kept within the bounds of reason if a careful fluoroscopic control is used.

5. *Mediastinal emphysema:* This is caused by air passing through the diaphragmatic hiati into the anterior or posterior mediastinum, often appearing in the neck. So far no deaths have been reported.

6. *Cardiac decompensation:* This results from distortion and displacement of the heart and great vessels producing an increased load on the heart. We have encountered this complication in a fifty-four year old man who showed electrocardiographic evidence of coronary sclerosis. I do not feel this complication will be important in patients who do not have a previously damaged heart.

The relative safety of therapeutic pneumoperitoneum having been demonstrated, I would like to present now the indications for penumoperitoneum, discuss them briefly, and present a brief study of our experience with its use at the Florida Tuberculosis Sanatorium.

INDICATIONS

1. The far advanced case to whom no other procedure is applicable. It is often wise to observe this type of case for a few months before instituting treatment. In order to obtain a beneficial result the patient

should at least be able to remain stationary on bed-rest alone. We have been surprised several times to see a fairly rapid downhill course stabilized and improvement start following the use of pneumoperitoneum.

2. Bilateral pulmonary tuberculosis with adhesive pleuritis preventing the use of pneumothorax. This is a large heterogeneous group with several modes of attack open. The vital capacity and general condition must be carefully considered. The patients in this group show phenomenal results, especially when phrenic nerve block is utilized as an adjunct to pneumoperitoneum.

3. Unilateral tuberculosis with adhesive pleuritis too acute or inadequately stabilized to make thoracoplasty advisable. Pneumoperitoneum is not expected to supplant major surgery in this type of case but rather to stabilize the lesion and prepare the patient for thoracoplasty. In some cases astonishing results will be obtained thus making a reversible procedure applicable to this type of case.

4. Predominantly basal lesions. Pneumothorax is still the treatment of choice; however, I feel that in this type of case pneumoperitoneum affords a direct means of attack with a low incidence of complications and very gratifying results. Basal tuberculosis has always been difficult to handle. It is too soon to predict but the results obtained would indicate the adoption of pneumoperitoneum and phrenic nerve block as the primary weapon of attack in basal lesions.

5. To enhance the effect of a paralyzed diaphragm. This indication requires little discussion. If an inadequate elevation of the diaphragm is obtained the desired result may be obtained by reinforcing the phrenic nerve block with pneumoperitoneum.

6. Uncontrollable haemorrhage. Often pneumothorax fails to control a haemorrhage because of adhesions. Pneumoperitoneum in combination with nerve block in this type of case often turns the tide. We have not encountered a massive haemorrhage in any case being treated this way. Also, in 7 cases the procedure has been successfully utilized to control repeated haemoptyses.

The above indications have been used at the Florida Tuberculosis Sanatorium for three years. We realize they are far from perfect but, at least, they serve as a workable beginning and through usage are gradually being revised so that therapeutic pneumoperitoneum may be properly placed as an adjunct in the scheme of collapse therapy. No one measure is always satisfactory. Instead, it is necessary to dovetail the procedures and to individualize so that each measure is instituted at the optimum

time. In such a program therapeutic pneumoperitoneum assumes its just position in the scheme of collapse therapy. The following results are therefore submitted for consideration.

RESULTS

Our series is only large enough to indicate the trend of results and is presented as a preliminary report to be supplemented and revised when sufficient time has elapsed.

So far, 56 cases out of 1,200 admissions have been given a therapeutic pneumoperitoneum at the Florida State Tuberculosis Sanatorium. This represents 4.7 per cent of all admissions. Forty-three cases are white and 13 colored. Fourteen cases, or 25 per cent, are known to be dead. Eleven cases, or 19 per cent, are unimproved. Thirteen cases, or 23 per cent, are improved, 6 of whom are now candidates for major surgery and are being prepared for some form of major collapse. One case is improved after thoracoplasty. The surgery has been completed so recently that a proper evaluation of the end-result cannot be made. Ten cases, or 18 per cent, are apparently arrested by pneumoperitoneum. Seven cases, or 12 per cent, are apparently arrested by means of major surgery in addition to pneumoperitoneum. Seventeen cases, or 31 per cent, are apparently arrested. Six cases had predominantly basal lesions, all are now apparently arrested. This is a small series but surely serves to show the importance of pneumoperitoneum in the treatment of basal lesions. Of the 14 deaths, 12 were far advanced hopeless and were treated because all other measures were deemed to be of no value. Twelve cases had had their disease and symptoms from two to seventeen years before admission.

Thirty-one cases, or 54 per cent, are apparently arrested or improved. Twenty-three of these cases had had symptoms for one year or less. This seems to indicate that the acute lesions of relatively short duration are more likely to respond favorably to therapeutic pneumoperitoneum than the long-standing chronic. Seven cases had treatment begun because of haemorrhage. All were controlled within a relatively short time, none dying from a fatal haemoptysis. Five are now apparently arrested and 2 are dead, the result of progressive disease.

SUMMARY

1. A general discussion of therapeutic pneumoperitoneum has been presented.

2. The indications have been discussed.

3. The complications have been discussed.

4. Statistics on 56 cases have been presented and the trend of results to be expected has been indicated.

SUMARIO

1. Preséntase una reseña general del neumoperitoneo terapéutico.

2. Repásanse las indicaciones.

3. Expónense las complicaciones.

4. Preséntanse estadísticas relativas a 56 casos, y se indican en general los resultados que cabe esperar.

TUBERCULOSIS IN STUDENTS

J. ARTHUR MYERS

In February, 1941, when one of my articles entitled *Tuberculosis in Students* appeared in the AMERICAN REVIEW OF TUBERCULOSIS, the editor seriously questioned and severely criticized it editorially. However, he has since kindly granted me the privilege of discussing his editorial and clarifying certain points in question.

Doctor Pinner questions whether miliary tuberculosis possibly occurs more frequently "*in youngsters who, three or four years previously, did not react to tuberculin*" than in those who were then reactors. The term "youngsters" is indefinite as to age. My paper concerned university students, among whom, according to our experience, his question is not pertinent. Indeed, we have now observed approximately a thousand students who became reactors under observation, not one of whom to our knowledge has developed miliary tuberculosis. Doctor Pinner says, "*In other words, can the knowledge of a positive tuberculin test help in foretelling or in forestalling the unfortunate outcome*?" There is no way to determine which of the tuberculin reactors will develop miliary tuberculosis; it happens in infancy, senility and at all intervening ages. Among infants and children, Wallgren found it more likely to occur during the first year of the infection than in subsequent years; however, it may and does occur many years after the initial infection is contracted. Certainly, one cannot question that it occurs only among those who have primary lesions. While the patient with well established miliary tuberculosis may react only mildly or not at all to the usual test doses of tuberculin, I have never seen a case that did not react if tested just before or during the onset of the disease. In any event, the tuberculin reaction indicates the potentiality. What has been said about miliary tuberculosis also applies to tuberculous meningitis and, in some degree, to tuberculous pneumonia.

Doctor Pinner quotes the following from my paper: "*Again, the student who reacts to tuberculin but in whom no lesion can be detected may at any subsequent time have chronic clinical tuberculosis. . . .*" He then says, "*But, is not exactly the same statement true for the student who does not react to tuberculin? Are there, then, justification and advantage in the advice that*

'those who react to tuberculin should be made thoroughly cognizant of the fact that they may develop clinical tuberculosis'." In our experience exactly the same statement is not true for the student who does not react to tuberculin nor is this statement true in earlier ages. In one group of children under our observation Ch'iu *et al.* found that, when 446 who reacted to tuberculin at the average age of seven years were followed for approximately eleven years, 15.02 per cent had fallen ill from clinical tuberculosis, whereas, of 772 who did not react to tuberculin at the average age of 6.6 years, but were followed approximately eleven years, only 1.68 per cent had fallen ill; in other words, approximately 9 cases of clinical tuberculosis developed among the tuberculin reactors to one among the nonreactors.

In our studies of tuberculosis among young adults, which consist primarily of students and graduates in nursing and medicine, we have made the statement that we do not know of a single individual with tuberculosis who did not react to tuberculin. Many years ago attention was called to the low incidence of tuberculin reactors among children in this section of the country and on numerous occasions and in many places we have emphasized the fact that 1 per cent or less of the children and adults become infected each year; therefore, during the entire span of life more persons receive their initial infections in adulthood than in childhood. Because of this fact, we long ago abandoned the term "childhood" tuberculosis and have since used "first infection type" or "primary" tuberculosis to distinguish between the disease resulting from the first attack of tubercle bacilli and that caused by reinfections. Indeed, it was this low incidence of tuberculin reactors among the children and young adults of this area that first caused us to insist upon periodic retesting with tuberculin of all who were nonreactors at any time the test was administered and to observe carefully those who became reactors under our observation, particularly during adult life. In fact, it was these studies which enabled us to describe the evolution of tuberculosis in the adult human body.

For a long time we have been advising both children and adults who do not react to tuberculin to be retested periodically, always informing them that at any moment they might contact a known or even an unsuspected case of tuberculosis and become infected. We have emphasized to them that only the tuberculin test will detect this infection in the majority of cases. Note the following quotations:

"All students who on the entrance examination react negatively to tuberculin should have the test repeated annually and every three to six months in case of any known exposure."

"Students who on retesting become positive tuberculin reactors should immediately be grouped with those who reacted positively on admission and treated in the same manner; that is, have an X-ray film examination of the chest at once and annually thereafter. Contrary to a general opinion of a few years ago, and one which is still extant, the young adult who becomes infected for the first time rarely develops clinical tuberculosis immediately. In fact, among those whom we have observed, the course of the disease has been essentially the same as that which we have seen among children when first infected, that is, the first manifestation of the disease is a positive tuberculin reaction; usually no significant symptoms are present. For the vast majority, the X-ray film of the chest is clear and remains so; for a small percentage within three to four months, the primary parenchymal focus may be visualized on the X-ray film. However, it nearly always comes under control without treatment."

For more than twelve years we have retested students of nursing and medicine who previously were nonreactors to tuberculin and this has been advocated regularly for other groups. Moreover, we have explained to them the potentialities of becoming infected or reinfected throughout life after leaving school and, thus, we have adequately covered the point which Doctor Pinner emphasized.

My article contained the following statement: "Those who react to tuberculin should be made thoroughly cognizant of the fact that they may develop clinical tuberculosis while in school or at any subsequent time in their lives; that even the period of senility is not safe from such development. There is no need to alarm them; they have come to the institution to obtain facts on many subjects, and facts concerning health are as important as those concerning any other subject. Having such health facts established in their minds and impressed upon them by an annual examination for tuberculosis should suffice to convince them that such examinations should be made throughout life."

Concerning this, Doctor Pinner says, "*It must require a well-nigh magical gift of persuasion to inform a student of the dire potentiality of his outlook, and to convince him at the same time that there is 'no need for alarm'.*" It requires only a common-sense discussion of the cause, evolution, treatment and prevention of tuberculosis with each student or even with groups of students; for the most part they are alert and the "magical gift of persuasion" is not necessary nor would it be well accepted by this type of mind. We do not discuss potentialities with reference to the development of acute fatal forms of tuberculosis, such as meningitis, miliary disease, and pneumonia, because in the past we have had no satisfactory

treatment for these conditions and also because they may develop almost over night. We do discuss at considerable length the chronic forms of tuberculosis, particularly pulmonary lesions, and emphasize to the tuberculin reactors of to-day that modern methods of examination are capable of detecting disease in the lungs long before they would experience anything but a sense of well-being. They are further informed that if this type of disease does make its appearance and is detected at the proper time it can usually be treated with little inconvenience to the individual so that it may be prevented from causing significant illness or becoming contagious.

The following sentence appeared in my article: "However, of those who develop primary lesions it has been estimated that as many as 25 to 50 per cent at some subsequent time have clinical lesions in one or more parts of their bodies."

Doctor Pinner quoted this sentence with a significant omission, as follows: "*Doctor Myers states 'that as many as 25 to 50 per cent of reactors at some subsequent time have clinical lesions. . . .'*" The omitted words, "it has been estimated that" were of great importance in this sentence. Doctor Pinner then asks what is the basis of this estimate and proceeds to give his own estimate. My statement referred to two reports which have been described in considerable detail elsewhere: First, that of Bogen, who has made an intensive study of this subject and concluded an article published in the August, 1940 issue of the AMERICAN REVIEW OF TUBERCULOSIS as follows: "Among those infected, the toll, though diminished, is still appalling. Mortality statistics, morbidity reports, autopsy examinations, tuberculin tests and X-ray surveys indicate that about half of all infected individuals develop clinical tuberculosis, and that from 10 to 20 per cent of them eventually die of the disease. The high risk of disease and death due to infection by the tubercle bacillus justifies increased efforts for its prevention." Second, our own observations on infected children kept under observation ten or more years reveal an alarming morbidity and mortality and, if estimates for the future are based on what has already occurred, more than 25 per cent of these individuals will be ill from tuberculosis before they have or should have reached the age of sixty years.

Doctor Pinner's statement with reference to 50 per cent of the population of this country reacting to tuberculin is only an estimate and is open to considerable question. He says, "*The age distribution at death is shifted considerably to higher ages, as compared to that of the living population; from this it follows that the population at death contains considerably*

more than 50 per cent reactors, and, hence, the chances of reactors to develop clinical tuberculosis are considerably less than 20 per cent."

Drolet has shown that the average age at which people died from tuberculosis in the registration area of the United States in 1913 was 32.5 years for women and 36.4 years for men, but in 1933 it was 35.8 for women and 41.5 for men. On the basis of what tuberculin testing has been done in this age period there seems to be much doubt as to whether 50 per cent would react typically to tuberculin if all were tested.

We are too likely to base our estimates on the findings in our three great cities, which in reality constitute only a small percentage of the total population of the nation. There are vast areas in this country where the incidence of tuberculous infection among adults is surprisingly low. Obviously, there is no time in life when an individual may not be infected or reinfected with tubercle bacilli but the program which has been recommended with reference to retesting nonreactors at all ages takes care of this situation.

Doctor Pinner says, *"Does tuberculin allergy spell only doom and danger? All well substantiated experimental work goes to prove that there is only one method by which the resistance against tuberculosis can be raised and that is by infection with tubercle bacilli, living or dead. It is inconceivable that the human animal should be the sole exception, and there are a good many observations, notably those by Heimbeck, that confirm for man the deduction from experimental studies."* How effective is this resistance when one realizes that it is only those who supposedly have it who fall ill or die from tuberculosis? No one has ever demonstrated a resistance capable of destroying virulent tubercle bacilli in the animal or all human bodies. What happens to the animals in whom this so-called resistance against tubercle bacilli is raised by infection with tubercle bacilli, living or dead, when they are reinfected endogenously or exogenously with a virulent strain of tubercle bacilli? Is the fact not well established that the resistance they manifest is only temporary and is apparent rather than real, since if they are observed sufficiently long each one falls ill and dies from tuberculosis? Who can say that the observations on BCG by Heimbeck will prove any more effective under the test of time than the method of von Behring, for which such exaggerated claims were made at the very beginning of this century? If a satisfactory resistance could be developed in animals, the veterinarians of the United States and Canada, after careful and prolonged trial, would not have discarded every method that has been described. Did not Krause and others show in a wholly satisfactory man-

ner that the apparent resistance which develops in animals and man through infection with tubercle bacilli is due to the fixing power of the tissues which results from allergy and that wherever tubercle bacilli are fixed they may proliferate, cause necrosis, and ultimate death of the animal or the human?

Again Doctor Pinner says, "*If Doctor Myers' concept were widely accepted, life insurance companies would logically refuse to insure reactors or accept them only as substandard risks, civil service would discriminate against reactors, the armed forces would have to reject them.*" It is of interest to know that this subject has already been before life insurance companies and some medical directors are convinced of the importance of administering the tuberculin test to all who apply for insurance. Indeed, it was presented and discussed before the American Life Convention in 1935, when the following statements were made:

"The positive tuberculin test of an applicant is of considerable significance, opinions to the contrary notwithstanding. We no longer look upon the test as an asset but as a double liability. This change in viewpoint has resulted from longitudinal studies of tuberculosis; that is, observations on the same groups of persons over long periods of time to determine what actually happens with reference to the development of clinical disease. A positive tuberculin reaction means that there is tubercle formation somewhere in the body and that living tubercle bacilli are present. While many persons with these tubercles go through life without developing clinical disease, it has recently been shown that such lesions are usually a potential danger throughout life.

"The medical director of a life insurance company recently told me that he plans to require a tuberculin test of every applicant in the future, regardless of age.

"Since we know that positive tuberculin reactors are more likely to develop clinical disease than negative reactors and since the percentage of positive reactors in many parts of the country is becoming smaller, it is obvious that we should keep all positive reactors under rather close observation through periodic examinations. This procedure is coming within the realm of physical possibility. This is extremely significant in that it enables us to diagnose the chronic forms of the clinical type of disease in an early stage. Chronic pulmonary tuberculosis often exists over a period of many months or even years before it causes symptoms sufficiently marked that the host feels the need of medical consultation.

"I believe that just as soon as the life insurance companies of this coun-

try require the tuberculin test as a part of the examination of every applicant the public will look upon the test with much more confidence than at present, and when insurance companies require a fluoroscopic or an X-ray film of the chest of every applicant who has a positive tuberculin reaction, the public will accept the X-ray as a part of every routine examination. Therefore, these two simple procedures added to the present examination for insurance will not only lead to the detection of many cases of tuberculosis who may not be insurable, but who may have their disease treated successfully, but will also be one of the most far-reaching steps that has ever been taken to control tuberculosis in the human family."

Any life insurance company could reduce its risks from tuberculosis by testing all applicants, retesting annually the nonreactor policy holders, and adequately examining all reactors for clinical tuberculosis.

Civil service already discriminates against persons who have some tuberculous lesions which can be visualized and would do well to give consideration to those who react to tuberculin but the location of whose lesions cannot be detected at the time of the initial examination.

There would be no necessity whatsoever for the armed forces to reject tuberculin reactors who do not have clinical lesions but it would be worth while for this country to administer the tuberculin test to all of the armed forces and those subsequently inducted into the service. The reactors should then be examined periodically for clinical disease in all parts of their bodies. The nonreactors should be retested periodically, not only to determine the source of any infections which occur but also to be informed of the potentialities in their bodies.

Approximately a quarter of a century ago a few persons in this country strongly advocated X-ray inspection of the chests of all persons who entered the army and navy during the World War. These were persons who had fundamental knowledge of tuberculosis but, unfortunately, others without such knowledge strongly opposed them; we know the result. X-ray inspection of the chest at the time of induction into service would not have entirely solved the problem for only evidence of gross pathology could then or can now be detected in this way. However, there were enough apparently healthy persons with gross lesions which could have been detected so that they would have been prevented from spreading their disease to fellow soldiers and sailors and many untimely deaths could have been prevented.

Since the World War the officials of our armed forces of that time have been severely criticised for not having screened from the recruits those

with gross tuberculous lesions. If the tuberculin test is not administered to the members of our armed forces now, there is a strong probability that within a quarter of a century, or even less, those now in charge will be the subjects of severe criticism.

The tuberculin reaction is the finest screen we have, and provides us with the first evidence of tuberculous infection. Therefore, it would serve not only to reveal potentialities among the members of our armed forces but also to trace the sources of bacilli among those who become infected while in service. It is just as logical to administer the tuberculin test to determine the potentialities with reference to tuberculosis among our armed forces as it is to do the Wassermann test to determine the potentialities with regard to syphilis.

Doctor Pinner says, "*It seems, then, that it would be wise to speak of tuberculosis as disease or as potential danger only when substantial reasons are demonstrable, and only when action to allay such danger is indicated and possible.*" This is exactly what we have done in the past; we have waited for signs, symptoms, X-ray shadows and laboratory findings before giving any consideration to the disease and this probably is the main reason the control of tuberculosis has been so slow. Destructive fires have small beginnings such as a spark, a match, or a cigarette; are we to wait until the forest is engulfed in flames or the occupants of the building are forced out before we declare the existence of a fire? If so, the salvage will be about equal to that of tuberculosis victims by the old methods of recognition of their disease.

In speaking of periodic examinations, Doctor Pinner says, "*But who can say to-day whether the young person with or without reaction is more in need of them?*" Obviously, the procedure we have advocated includes both the reactors and the nonreactors of to-day. Whether an individual reacts to-day or a year from to-day, he must be placed in the group to receive careful examinations at least annually as soon as he is known to be a reactor. Certainly it is beyond question that those with tubercle bacilli in their bodies, as manifested by the tuberculin reaction, are the persons to be observed carefully for the development of clinical tuberculosis.

DEMONSTRATION OF TUBERCLE BACILLI

Relative Value of Various Methods of Detecting Tubercle Bacilli.—When is Sputum Negative?

Results of a Panel Discussion before the Medical Section of the American Trudeau Society, Tuesday, May 6, 1941, San Antonio, Texas

Emil Bogen, Olive View, California, Chairman

Panel: S. A. Petroff, New York, New York
Joseph E. Pottenger, Monrovia, California
Henry S. Willis, Northville, Michigan
Max Pinner, New York, New York
Henry C. Sweany, Chicago, Illinois

Support expressed is shown in parentheses after each measure. ⁂ represents the Chairman, * members of the panel, a, audience.

1. *Specimen collected:*	Morning specimen (*)
	24-hour collection (**** ⁂)
	14-day accumulation (*)
	Adapted to individual conditions (*a)
2. *Portion to be examined:*	Selected particle (**)
	Concentrated sediment (** ⁂)
	Concentrated flotation (*)
3. *Digesting agent:*	Antiformin (a)
	Weak alkali (*)
	Strong alkali (*** ⁂)
	Mineral acid (*)
	Oxalic acid (*)
	Tergitol (*)
	Caroid ( )
4. *Staining solution:*	Petroff's (*)
	Ziehl's (*** ⁂)
	Cooper's (**)
5. *Counterstain:*	Methylene blue (**** ⁂)
	Brilliant green (*)
	Picric acid (*)

6. *Fluorescence microscopy, light source:*	Carbon arc ( ) Mercury vapor lamp (⁂) Filament bulb ( )
7. *Tube preferred for gastric lavage:*	Large (Ewald) (**) Small (Levine) oral (**) Small nasal (**⁂)
8. *Volume of water for gastric lavage:*	None (*a) Less than two ounces (**⁂a) More than two ounces (***a)
9. *Culture media used:*	Petroff's (*) Corper's egg yolk (**) Jensen's Petragnani or other modifications of Petragnani (****⁂) Saenz' Loewenstein (****⁂)
10. *Route of inoculation into guinea pigs:*	Intratesticular (*) Intracranial ( ) Intraperitoneal (a) Subcutaneous (*****⁂)
11. *Early diagnosis from guinea pig:*	Tuberculin test (****⁂) Aspirate lymph nodes (****⁂) Smear local lesion (*) Hasten lesion with silica or other material ( )
12. *How long should one slide be examined:*	Two minutes (a) Five minutes (**) Ten minutes (***⁂) Fifteen minutes (*) Hours ( )
13. *How can avirulent acid-fast bacilli be differentiated from tubercle bacilli:*	By individual morphology and stain (*) By cultural characteristics (****⁂) By animal inoculation (*****⁂) By clinical evaluation alone (*)

14. *How often should routine sputum examinations be repeated in positive sputum cases on rest treatment:*	Every week (a) Every month (**) Every three months (*** ℀) Every six months (*) Not as routine (*)
15. *How should sputum conversion be verified:*	Repeated direct smears (*) Repeated concentrates (**) Culture or guinea pig (**) Repeated cultures (*** ℀) Gastric lavage (*** ℀) Repeated gastrics (a)

BOOKS

HENRY C. SWEANY: *Age Morphology of Primary Tubercles. Pp. xxii + 265, with 73 plates, 1941, Charles C. Thomas, Springfield, Illinois, fabrikoid, $5.00.*

By KORNEL TERPLAN

This monograph is based largely on postmortem material exceeding 900 lung specimens. Only in the latter part of the study were postmortem X-ray photographs taken routinely "of all principal portals of entry." Originally this procedure was used in such cases in which the antemortem (clinical) roentgen film failed to demonstrate lesions clearly. For the most part, only lesions judged as primary tubercles are studied and the relationship between their morphological structure and their estimated age is recorded. Most of the examined tubercles were in an advanced state of healing and calcified. The lung specimens were fixed and serial gross sagittal sections made of about one centimetre in thickness. On an average, seven foci of each case were examined. Where the lesions were present in large numbers, only part of them were studied. After proper decalcification, the tubercles considered to be primary were then analyzed, according to the so-called "age formula." Each tubercle was arbitrarily divided into two parts, the centre and the capsule. According to the different age, early, middle and late, evolutionary changes were studied. The early changes, in all but very young tubercles, comprise exudation, proliferation of monocytes and lymphocytes and caseation. In the middle and late changes the structures of the inner, a middle (added by the author), and of the outer capsule were analyzed: extent and degree of calcification; resorption phenomena of the core and the capsule; replacement fibrosis; hyalinization; appearance of fibro-osteoid tissue with islands of calcification; bone formation with or without lymphoid marrow. The author assumes that early and late evolutionary changes take place according to an accurate time schedule.

The core and the capsule of each tubercle are assigned a "maximum area value" of ten. For both core and capsule the maximum quantities of the above listed structural changes, like capsule formation, caseation, calcification, bone formation, named by the author as "ingredients," are also expressed as ten. In estimating calcification, extent and density as visualized on the X-ray film are used, along with the histological picture. It is beyond the capacity of the reviewer to dwell on further details of this comparative analysis of the structures forming primary foci. Their evaluation and estimation are admittedly on a highly subjective basis, and the reader is referred to the schemes

and tables in the book, although it is possible that he might become confused by them. It should be stated, however, that this method was not applicable to small or large lesions. It was found most suitable for tubercles from 3 to 11 mm. in diameter. The author admits that his method is perhaps too complicated for common use. In cases in which the primary tubercle is too small, or where it could not be found, lesions in the lymph nodes which formed part of the primary complex were used. The author includes under the term "primary tubercle," as a rule, a number of lesions in the lungs and in the lymph nodes. Not infrequently he encountered 5 to 15 components having the same age characteristics.

With the so-called "age formula," the material is examined according to different groups. In the two leading chapters, 30 cases are described in all of which the time of contact with a possible source of tuberculous infection was well established and had begun and ended in childhood before the seventh year of age. The other chapter deals with 100 cases in which accurate case histories of contact were known at any time during life. The age of the primary tubercles in this series was estimated from 0.1 to 19 years. The same method then is also applied to the age determination of calcified tubercles in the spleen, although bone formation was found in only one case. In the second part of the monograph this principle is practically applied in an attempt to determine the time of infection in a miscellaneous group of cases including nurses, hospital attendants, and also a few cases with presumptive changes of reinfection-tubercles. The final chapter deals with the age criteria of tubercles as revealed on roentgen films of patients. The X-ray demonstrations of the opaque circular shadow, produced by a bony shell around the more white and dense calcification centre in the very old tubercles, are very illuminating. The book contains 73 tables with illustrations, mostly of histological lesions demonstrating various states in the evolution of tubercles, in addition to a considerable number of X-ray films of specimens and a series of clinical films. Almost all of these are of very good technical quality. So are the photographs of gross specimens and the technically excellent reproductions of numerous microscopical lesions.

The author claims in his introduction that no consideration had been given so far by pathologists to the correlation of anatomical changes to the time factor. With this statement the student of the tuberculosis literature will disagree. True, no one has ever tried to prescribe an "age formula" of such a specific, arithmetical type as Doctor Sweany has presented here. This formula is the more surprising as Doctor Sweany seems to be, in general, aware that the process of healing is influenced by a variety of factors. A primary lesion will heal probably more rapidly wherever it is single and restricted than in cases in which it forms the source for a more or less direct extension of tuberculous disease within the lung. We also know very well, on the basis of careful

studies of Ghon, Schuermann, Huebschmann and others, that the primary focus may heal completely and fairly quickly, while in some lymph node components of the primary complex a chalky or even a caseated state might persist for a long time. In spite of this, lymph node lesions were frequently used by Doctor Sweany in determining the age of the primary tubercles. That ossified, firmly petrified states of old tubercles indicate a relatively old age of such lesions, has been known for a long time, emphasized especially by Ribbert, Lubarsch and Ranke, and used to prove their primary character relative to less old lesions. We also should remember Ghon's careful statement: initial late primary infections heal in the same manner as initial childhood infections; it is difficult on the basis of anatomic changes to determine the time of the first infection. The table of Schuermann shows stony tubercles in 26 per cent below the eighteenth year, but in 62 to 91 per cent between the eighteenth and eightieth years. The sequence of events in the eventual repair of the original caseated primary tubercle does not follow in all cases a rigid pattern. For instance, capsules, after having been formed, do not necessarily disintegrate by caseation. They may remain hyalinized for a long time.

What any student of tuberculosis misses most painfully in a monograph dealing with morphological changes are clear, complete anatomical reports in accepted anatomical terms. This applies likewise to the histological descriptions. From the anatomical findings given, it is impossible to prove whether or not many statements made relative to pathogenesis are correct. With the greatest ease a "moderate lesser circulation spread to the lungs" is distinguished from a slight but recent "major circulation spread to lungs, spleen and liver;" or we read of "tubercles in the diameter of the cerebellum," of "fibrous tissue with several distinct fibers of about 30 per cent maximum thickness," or of "an original lesion which was not found but which would, no doubt, have shown more calcification;" or, referring to the history of a patient, of a "nervous breakdown as the result of cerebral metastases as well as manifestations of toxicity;" or again, of "postmortem findings on calcifications which were not large enough for study." The term "primary lesion" is used very freely; also that of "multiple primary." Doctor Sweany claims he has found 5 to 15 parenchymatous components of a primary lesion not infrequently and believes this result is due to the more accurate method of search afforded by X-ray. Here, again, the reviewer is inclined to agree rather with the more conservative figures of Ghon and Blacklock. Or we read of "a small primary infection in the right base which spread up the bronchus as well as through the diaphragm, causing a slight peritonitis" or of "secondary calcifications," *et cetera*.

It should have been expected that among 900 cases some complex of a reinfection would occur. Doctor Sweany mentions one of these observations, though complicated by large cavities in both lobes, but curiously, exactly for this phenomenon for which the different structural age is the deciding issue,

he claims it is difficult to find adequate evidence for proof. No morphologist will follow Doctor Sweany in postulating occult extrapulmonary primary lesions without proving these or primary tubercles in the lungs which were resorbed completely. Doctor Sweany assumes quite freely that no structural traces might be left in the parenchyma. Again this has not been proved as yet. In a highly interesting observation of a possible true reinfection (case 159), all detailed anatomical reports are lacking. These alone could prove the author's conception. Finally, there are some statements with which pathologists most familiar with tuberculosis in man will disagree: that only about two-thirds of the primary lesions of tuberculous patients are present at death and perhaps fewer of these lesions in patients dying of other diseases than tuberculosis. Especially for the latter group, the reviewer's own figures show that with insignificant exceptions the primary tuberculous lesion in the lung parenchyma leaves a permanent, usually obsolete, petrified focus or, rarely, a fibrous scar.

No word is said as to ossified lesions which are not of tuberculous nature (the so-called osteomata in the literature). On the other hand, we read that there is no absolute way to differentiate old phleboliths from very old tubercles. As firm old phleboliths always were found by this reviewer to be firmly surrounded by a vessel wall, the differentiation between phleboliths and petrified tubercles seemed very simple in all cases.

Some quotations from the literature are not sufficiently specific or even not accurate. Puhl *has* mentioned, regarding the age difference between primary and reinfection foci, that the latter might not be ossified because they frequently are acquired at a much later age.

This reviewer highly appreciates the great enthusiasm which must have been the impetus for putting the large material together. He also is too well aware of the delight which morphological studies of tuberculous lesions, especially at different points of their gradual evolution in different structural phases, can impart. Many age determinations in terms of years of some of these lesions very well might be correct. On the other hand, in tuberculosis, as well as in other diseases, there remains a highly individual factor which might greatly change any accepted, rigid scheme like the so-called "age formula" of Doctor Sweany. This might apply especially to actually tuberculous cases while, in individuals in which primary complexes are entirely incidental findings, comparative studies as to the age of such lesions might at least eliminate the disease factor. Only in those cases in which the time of the first infection is known beyond any doubt, possibly corroborated by an early positive tuberculin reaction, is the eventual morphological analysis of the remnants of the primary tubercle a reliable indicator of the actual and structural age. Contemplating the unusually large material presented in Doctor Sweany's book, this impression remains with the reviewer, that progress in our knowledge of

tuberculosis in man is better served by most thorough analysis of a smaller material than by using many hundreds of cases, the available reports on which do not convey, neither in substance nor much less in form, those clear, hard anatomical facts on which alone any morphological study should be based. The terminology often does not conform to accepted standards in morphological research.

LAWRASON BROWN: *The Story of Clinical Pulmonary Tuberculosis. Pp. ix + 411, Baltimore, The Williams & Wilkins Company, 1941, cloth, $2.75.*

By MAX PINNER

Of all the historical treatises on the development of our knowledge of tuberculosis, this is probably the most living, pulsating story. More than any other known to this reviewer, it is a book of humanities and humaneness. More than any other, it is personalized history, personalized in a double sense because it bears the unmistakable imprint of Doctor Brown's mellow and wise personality and because it shows the heroes of the story not only as scientists, researchers and great clinicians but as human beings in work and personal contacts.

The unique distinction of Doctor Brown in this book seems to me to lie in the fact that he not only discusses the milestones of the development, such as Waldenburg, Predöhl and Flick do, but he reveals with deep insight some periods between the milestones. He not only, as an example, stresses and explains the importance of Laennec's work, but he traces carefully the influence of his work on his contemporaries and the next generations. Thus, Doctor Brown shows many extremely important historical details and *curiosa*, many of which are little known. But precisely these facts make for continuity and unbroken flow.

The title of the book is peculiarly felicitous and pertinent. It is a story and not a history. It is written in the style of the *causeur* in the grand manner and not the style of a historical treatise. And, in spite of this, it is an erudite book which must be based on innumerable hours of patient research. And it deals definitely with *clinical* pulmonary tuberculosis, or rather it is the story of pulmonary tuberculosis seen through the eyes of a great clinician. In this sense, the omissions are quite significant. Anything that does not directly go into the building of the clinical picture is either not mentioned at all or is treated according to its marginal importance.

Mrs. Brown, to whom great gratitude is due for the editing of Doctor Brown's lectures, papers and notes, states in the Preface that "much has been eliminated that would be of interest only to a few." Taking the intimate details in the book as a sample, one wonders whether the "few" are not many, since it is with real regret that one approaches the last pages.

Dr. Homer L. Sampson has contributed an interesting chapter on Diagnosis by X-ray and Dr. Edward W. Archibald has written a fascinating and well balanced chapter on the Development of Surgical Methods in Treatment.

Something should probably be mentioned of the unique approach used in chapters 2, 3 and 4 that are headed The Visit in 1700, The Visit in 1800 and The Visit in 1900. But, not unlike a reviewer of crime stories, I feel that it would be almost unfair to the prospective reader to lift the veil—let him see for himself.

Much of the book is as readable for the layman as for the physician. Even the reader well familiar with historical phases will get additional information in regard to facts and certainly in regard to attitudes and analyses, and none will fail to admire the organic unity of Doctor Brown's presentation and the conversational fluency of his narratives.

GRACE M. LONGHURST, with the collaboration of N. STANLEY LINCOLN, BERNICE E. TANSEY AND CAROLINE T. WHITE: *Tuberculosis Nursing. Pp. 280, with 67 illustrations, Philadelphia, F. A. Davis Company, 1941, fabrikoid, $3.00.*

By LEWIS J. MOORMAN

This very timely manual contains an instructive and impressive foreword by Dr. Robert E. Plunkett, also a preface by the author, which calls attention to the fact that the book has been written for nurses and student nurses interested in the institutional care of the patient, and not in field work in public health. The preface suggests that the text has been prepared with the greatest care and that the manuscript was submitted to various authorities in the field of medicine and nursing for criticism and suggestions.

In addition to the foreword and preface, there is an index of illustrations, a table of contents, and a general index. The arrangement of the text shows the following eight units or divisions: (*1*) Clinical Tuberculosis; (*2*) Aseptic Technic; (*3*) Nursing Care; (*4*) Chest Surgery; (*5*) Behavior Problems; (*6*) The Discharge and Rehabilitation of the Patient; (*7*) The Out-patient Service; (*8*) Nursing Care in Extrapulmonary Tuberculosis.

There are from two to eight chapters under each unit, making a total of twenty-six. At the end of each unit there are questions for review and a well selected bibliography for supplementary reading. The author's diction and straightforward style make reading easy.

Among the numerous illustrations are to be found several isotype charts taken from publications of the National Tuberculosis Association. Many of the illustrations are of great educational value, but the reproductions of X-ray films of the lungs are not adequately described either in the text or the legends which appear under each illustration. Nurses and student nurses

who have not had training in the interpretation of roentgenograms of the lungs will not get much help from these pictures without the aid of someone who has had such training.

The chapters on Clinical Tuberculosis, Aseptic Technic and Nursing Care are well done. In the chapter on classification, symptoms, diagnosis and complications, the author copies freely from the 1940 edition of *Diagnostic Standards and Classification of Tuberculosis*, published by the National Tuberculosis Association. In this chapter the designation of tuberculosis in other organs and tissues of the body as complications of pulmonary tuberculosis might be questioned. It would seem more logical to refer to these as associated lesions or extensions of the tuberculous condition to other parts of the body.

The chapters on general nursing care and nursing care of complications are presented, and it is most gratifying to find three chapters devoted to behavior problems of the tuberculous patient. One deals with the nurse's attitude toward the patient, and two present case histories of patients handicapped by psychological conflicts. In these chapters the author manifests a remarkable insight and a broad understanding of these conflicts and the resulting maladjustments. The case histories are wisely chosen and effectively presented. The careful analysis of individual cases with a keen appreciation of the wide range of personality traits and their influence upon the patient's reaction to environment, is most commendable and will be of great value to both nurses and patients.

When we consider the scope of this little book, and the difficulties encountered in an effort to convey in a few words adequate knowledge of such difficult subjects as clinical tuberculosis, aseptic technic and chest surgery, we think it remarkable that the author has so well performed her task. But, student nurses and many graduate nurses are sorely in need of a more thorough knowledge of the anatomy, physiology and pathology of the lungs. It is to be regretted that the book does not contain a brief discussion of these fundamental subjects, with special application to the problems at hand. With such a background, students could more easily and more adequately grasp the difficult problems presented. These deficiencies, some of which are unavoidable in such a manual, can be largely overcome by supplementary knowledge, to be supplied by a faithful perusal of the excellent books listed at the end of each unit and by good teachers.

Chapters dealing with instructions to the patient and his family, and rehabilitation, are very instructive. There are also chapters on the out-patient service, including chest clinics and clinic routine. The book closes with a discussion of nursing care in extrapulmonary tuberculosis.

The author and her collaborators have succeeded in bringing together in one small manual a remarkable store of valuable information. Nurses and doctors

interested in tuberculosis, in and out of institutions, should read this valuable book.

JESSAMINE S. WHITNEY AND HELEN JANE STOFER: *Tuberculosis among Nurses. Digest and Discussion of Recent Articles. Pp. 31, National Tuberculosis Association, New York, 1941, paper.*

By MAX PINNER

This is an excellent and most useful summary of papers on Tuberculosis in Nurses that have appeared between 1935 and 1940. It is, of course, an extremely important topic and one that contains many possibilities of further elucidating unsolved problems in epidemiology and pathogenesis. The reader must be impressed by the extreme divergence of opinions expressed by the various authors, and this study does little, by necessity, to resolve the conflict and rather more to bring it into sharp relief. One can hardly escape the impression that many of the interpretations (of the original authors) bear the mark of wishful thinking.

It is probably a fairly acceptable summary, on the basis of the data presented, to say (*1*) that among nurses (especially among student nurses!) the conversion rate from nonreactors to reactors to tuberculin is considerably greater than among a comparable population not engaged in nursing; (*2*) that the morbidity rate is slightly or moderately greater; and (*3*) that the fatality rate of diseased nurses is considerably smaller and that the mortality rate is probably smaller than in any other population group. An obvious corollary of the third statement is the fact that nurses are supervised more carefully, diagnosed earlier and treated more promptly. This, at least, is the ideal situation which can and should be realized.

All papers quoted are explicitly or implicitly concerned with the one question: *Is the nursing profession more endangered by tuberculosis than other comparable groups of the population?* Unavoidably, the answers show extreme discrepancy because they are based either on tuberculin conversion rates, or on morbidity rates or on fatality rates or on mortality rates. It is up to the author to choose his method of approach—each of the four methods is justified, but—and this, at times, is not only overlooked but practically obscured—each of the methods has a different degree of significance and carries different weight of conviction. It does not seem intellectually fair to attack the statement that the mortality rate is low by showing how high the tuberculin conversion rate is.

The present study is valuable not only as well compiled source material, but especially because it contains many analyses and criticisms of methods used in assembling the raw data. The definitive critical study of all available

data (and therewith the final answer) is still to be done and must undoubtedly wait for a broader material, longer observation periods—and, finally, for an author who will with complete objectivity denude the published papers, wherever necessary, of unsound methods and tendentious conclusions. In the meantime the study by Miss Whitney and Miss Stofer provides a most welcome and easy way to get acquainted with the present unsettled—and undoubtedly temporary situation of the question.

CHARLES WEYL, S. REID WARREN, JR. AND DALLETT B. O'NEILL: *Radiologic Physics. Pp. xvii + 459, with 166 figures, Charles C. Thomas, Springfield, Illinois, 1941, cloth, $5.50.*

By KENNETH S. COLE

The authors of *Radiologic Physics* are on the staff of the X-ray Laboratory, Moore School of Electrical Engineering, University of Pennsylvania. This laboratory has had considerable support from the National Tuberculosis Association for its active research on physical problems of X-ray therapy and diagnosis and for the past ten years it has also conducted a physics course for radiologists. This book, although intended primarily as a text, is a result of both activities.

In the first half of the book fundamental concepts of physics and electrical engineering are developed and applied to radiological equipment. In the second half a discussion of the nature of radiation and the phenomena of X-rays and radioactivity leads to therapy and diagnosis. Here the measurements and use of radiation for therapy and fluoroscopic and radiographic techniques are discussed from the physical view-point. An outline of algebra, trigonometry and calculus and mathematical tables are given in the appendix.

Radiologic Physics is an introduction and guide to principles and to subject matter. It is broad at the expense of detail, and indeed there are no detailed descriptions, derivations or diagrams of theory, experiment or practice. Consequently the book is not a technical handbook for any branch of the field it covers and it is easy to criticize the authors for their choice of material. This reviewer for example would favor more emphasis on the physical aspects of radiation and less on alternating currents. However the general reader is well prepared for current periodical literature and excellent references provide ample range for the more inquiring students. The book is well written and well made.

JULIO PALACIO AND EGIDIO S. MAEZZEI: *Tumores primitivos malignos broncopulmonares. Cancer—sarcoma—linfogranuloma. Pp. 401, with 129 figures and 4 colored plates, Editor: El Ateneo, Buenos Aires, 1940, paper.*

By B. M. FRIED

Our confreres in South American like ourselves were impressed with the "alarming" statistical increase of carcinoma originating in the lungs. Their figures based on autopsy material collected since the beginning of this century showed that within the last four decades cases of bronchogenic cancer have increased fivefold. The authors do not venture to state in a dogmatic way the possible cause or causes for this peculiar phenomenon. Interestingly, in the Medical Clinic of Prof. Mariano R. Castex (in whose Department the investigation was conducted) cancer of the bronchus is observed as frequently as that of the stomach. It is also noteworthy that 94 per cent of their patients were males while only 6 per cent were females.

The microscopical classification of bronchogenic cancer, as given by various American and Continental pathologists, is reviewed and the conclusion is reached that the only difference between investigators is that of nomenclature. They accept the view that the tumor is essentially one of the bronchus originating *en parte* from the so-called basal cells of the bronchial mucosa.

Macroscopically they differentiate six varieties: nodular, massive, pleural, mediastino-pleural, circumscribed and apical. The last named, which produces the so-called Pancoast syndrome, is described in some detail.

The clinical forms of the disease are discussed at some length. Attention is called to *canceres latentes* which is equivalent to our occult or silent carcinomata. The authors classify their cases into: stenosing, acute, pseudotuberculous, cystic, suffocative, haemorrhagic, pseudopleuritic, pleuritic and cavitary. The symptomatology of the various types is detailed and illustrated with clinical cases. Over 40 pages are devoted to discussion of metastases, particularly to the central nervous system. Clinical protocols are cited at some length to illustrate the various manifestations caused by the deposit of malignant cells in the brain.

A large section of the book is devoted to the radiological aspect of the disease and is illustrated with 80 roentgenograms. The use of serial bronchography, as advocated by Pedro L. Farinãs of Havana, Cuba, and tomography is stressed. It would appear, however, that these methods are still in a rudimentary stage and are rarely of assistance in making an early diagnosis of malignant pulmonary disease. Bronchoscopy and the importance of obtaining a biopsy are discussed. Importance, too, is attached to the morphological examination of the sputum and the pleural exudate for the presence of malignant cells. Treatment is very briefly detailed. A few pages are devoted to pulmonary sarcoma and lymphogranuloma. The bibliography is nearly exhaustive, embracing some thousand titles.

The monograph is a handsome volume which denotes craftsmanship and good taste of the publishers. It also indicates scholarship on the part of the authors.

ALEJANDRO A. RAIMONDI AND RICARDO SCARTASCINI: *La atelectasia en la tuberculosis pulmonar. Pp. 242, with 60 illustrations, El Ateneo, Buenos Aires, 1938, paper.*

By B. M. FRIED

The problem of massive collapse of the lungs interested observers nearly a century ago. Mendelsohn, in 1844, Traube, in 1846, and Lichtheim, in 1879, studied the question experimentally by obstructing the bronchial lumen of dogs. Not only the gross anatomy of the disease but the physiology as well were studied by the older investigators. Thus Lichtheim investigated the exchange of gases in the collapsed lung and his figures compare favorably with those found by modern observers.

The problem was neglected for decades. In 1910 William Pasteur published his observation on *Active Lobar Collapse of the Lung after Abdominal Operation.* Pasteur's article stimulated investigators, particularly Americans, who elaborated the problem. That atelectasis occurs with some frequency in pulmonary tuberculosis had been known since Farris published his article in 1925. The literature of the past fifteen years abounds in reports on this subject.

The monograph by Raimondi and Scartascini is a comprehensive summary and discussion dealing with virtually all aspects of the problem. Their definition of the phenomenon is orthodox: A lobe or an entire lung is considered atelectatic when it does not contain any air and is markedly reduced in volume and functionless. Atelectasis in pulmonary tuberculosis may result from endogenous causes such as a copious haemorrhage (posthaemoptoic) or from exogenous factors such as transbronchial migration of tuberculous lymph nodes or of caseous fragments. In many cases the cause cannot be determined.

The monograph is divided into ten chapters. The physical laws, the exchange of gases and the various forms of atelectasis are discussed and illustrated by case reports. The symptomatology and methods of diagnosis are given due space. A chapter is devoted to the influence of collapse therapy on pulmonary atelectasis and another to the influence of atelectasis on tuberculosis of the lung.

The book is clearly written, beautifully printed, profusely illustrated with roentgenograms and is provided with an extensive bibliography following each chapter.

JOSÉ SILVEIRA: *O problema da atelectasia nas suas relações com a tuberculose do pulmão. Pp. 189, with 79 figures, Bahia, 1940, paper.*

By B. M. FRIED

Silveira, apparently to justify his publication, quotes Jacobaeus who wrote: "The discussion on the occurrence of atelectasis, its frequency and significance

in pulmonary tuberculosis is far from finished; for many decades to come it will no doubt be in the center of lively discussion among clinicians as well as pathologists." Silveira's treatise hardly needs an apology. His book is a distinct contribution. The matter is presented in a scholarly and competent manner. He is thoroughly versed in the North American and continental literature, and he renders unto Caesar what belongs to Caesar...

Each chapter, five in all, is prefaced by a concise summary. Chapter I, for example, on fundamental notions of atelectasis, is summarized thus: *Atelectasis: the etymology of this word and its synonyms; the necessity for a uniform and clear terminology. The fetal lung and atelectasis; ideas of former writers; personal interpretation. Atelectasis and pulmonary tuberculosis. Atelectatic collapse. Definition of atelectasis.* In the other chapters the author elaborates on the diagnosis, the rôle of tuberculosis in the genesis of atelectasis, the clinical forms of atelectasis, the rôle of atelectasis in the evolution and healing of tuberculosis.

The monograph is illustrated by macro- and microphotographs and by a considerable number of splendid roentgenograms. The bibliography is made up of the most representative articles of the world's literature.

M. BENMOSCHÉ: *A Surgeon Explains to the Layman. Pp. 317, with many diagrams by Bhola D. Panth, 1940, Simon and Schuster, New York, cloth, $3.00.*

As Reviewed by a Surgeon
By ARTHUR H. AUFSES

The author takes an entire chapter to justify the need for his handiwork. He admits that there are definitely two sides to the question, "how much should the layman know about surgery." This reviewer is one of that group which believes that the average patient should know as little as possible. In my opinion the best patient is the one who knows the least about his condition but has the utmost confidence in his physician and surgeon; so much confidence that he limits his questions to bare necessities. I must also disagree with the author when he states that ordinarily the patient wants to know something about the details of operations. It is my experience, gathered in twenty years of active surgical practice, that the patient usually asks no more than the following questions: How long will my scar be; will it show; is the operation dangerous; how long will I have to be in the hospital; will I be cured; when will I be able to go back to work, and how must will it cost?

The author states that many people needlessly fear the surgeon's scalpel and he believes that if surgical procedures were explained to them in simple language, their fears might be dispelled. I believe that such a type will only be made more fearful when the details are pictured for him.

The person who refuses surgery because of religious beliefs surely cannot be

enticed into the operating room by descriptions of the necessary operation. Too many of them have gone on to die or have watched their relatives pass on without benefit of surgery merely because of their fanatical beliefs. Surely, the individual who travels through life with an unsightly wen on his scalp must have had the simplicity of the operation explained to him on frequent occasions. He may have some peculiar aversion to surgical procedures based upon superstition, ignorance or untruths he has heard. But let the tumor become inflamed and cause him severe pain and he will quickly submit to surgery for relief of his discomfort. In the same manner, a really painful, prolonged attack of gallbladder colic will do more to convince a patient of the need for surgery than any description of the operative procedure.

As for the book, it is very well written and undoubtedly serves the purpose for which the author intended it. The eminent surgeon who wrote the foreword stated that "it is not at all intended for the surgeon." With this I can heartily agree, and must admit that I had difficulty in finishing a few of the chapters describing every-day operations in the layman's language.

Even though the operative descriptions are as simple as possible, I am afraid that they are still outside of the grasp of the average reader. Surely, the layman must become quite confused in attempting to understand the details of a hernial repair, or the two different methods of removing the gall-bladder. And as for the intricacies of a gastro-enterostomy, I am certain that many a physician or specialist (nonsurgical) would not be able to follow the various sutures even though they are painstakingly described.

For the surgeon, the book is a pure waste of time. For other members of the medical profession, who for many years have not been in contact with these simple every-day procedures, it may have some appeal. As to its reception by the layman, for whom it is primarily intended, I, as a surgeon, find it impossible to render an opinion.

M. BENMOSCHÉ: *A Surgeon Explains to the Layman. Pp. 317, with many diagrams by Bhola D. Panth, 1940, Simon and Schuster, New York, cloth, $3.00.*

As Reviewed by a Layman

By LEO M. FRIEDMAN

Had Doctor Benmoschè found time during the Teeming 'Twenties to explain surgery to the layman he would have earned no small reputation as a discerning critic of American folkways. For, during those years, everybody who was anybody had an operation. This craze (mostly for appendectomies) may have served no medically sound or useful purpose but it did help make conversation in considerable quantities. Laymen tirelessly matched scars and stories of their experiences under anaesthesia and the scalpel, and frequently it was

difficult for the listener to determine when, if at all, the effects of the anaesthetic had worn off. Against this background of the appendix, who can dare imagine what cultural heights might have been attained had the lay public been more generally aware of the surgical possibilities inherent in the digestive system, the excretory system, etc.

But coming at a time when the world is older, sadder and, perhaps, wiser, *A Surgeon Explains to the Layman* represents a positive and valuable addition to the reader's understanding of the vital rôle which surgery can play. In simple and understandable terms, and with far more restraint than the average motor car manufacturer uses to describe the whys and wherefors of his latest model automobile, Doctor Benmosché explains the reasons behind and the techniques of surgery.

This is no romanticized account of the work of the surgeon. Its purpose, in the words of the author, is to help dispel "through greater understanding that unnecessary and heartbreaking fear which surrounds the word 'operation.'" In this it succeeds. For the most part, Doctor Benmosché has treated his subject in an interesting fashion, avoiding oversimplification of his material on the one hand and involvement in strictly technical terms on the other. In this respect he has avoided the pitfalls ordinarily besetting any author who undertakes to explain a technical subject to the layman.

From the standpoint of this layman, certain of the drawings used to illustrate operations might have been clearer, and a brief dictionary of the most frequently used technical terms should deserve a place.

The March of Medicine. New York Academy of Medicine Lectures to the Laity, 1940. Pp. xii + 154, New York, Columbia University Press, 1941, cloth, $2.00.

By EDWIN L. DEMUTH

This book is number five in the series of the New York Academy of Medicine Lectures to the Laity. Its six chapters are compact, clear and well-rounded. As Doctor Solley points out in his introduction, the authors describe not only a fact, but a "definition of its significance, or of its relation to the body of knowledge already possessed." This interpretive rather than reportorial approach lends both charm and depth to the subjects presented. Each of the authors, but particularly Doctor Myerson in his chapter on *The Inheritance of Mental Disease*, stresses the philosophy of medical science. There are enough technical terms to make the lectures scientific, yet not too many to make them unintelligible to the layman. *The Romance of Bronchoscopy*, by Doctors Chevalier Jackson, Senior and Junior, gives a good history of this procedure, its difficulties and the changing indications for its use. Although in parts of

the book there is an element of the dramatic, there is no attempt to gloss over the failures or avoid the unsolved problems of medicine. Instead, there is throughout a wealth of factual data, presented with a breadth of vision which is both challenging and satisfying.

Each of the authors is an outstanding leader in his specialty, and undoubtedly his position in the world of medicine is made known to his listeners at the time of the address. For the readers of the printed speech, a short biographical sketch at the beginning of each chapter might lend even more weight to the ideas presented than the excellence of the thoughts themselves. The book is to be highly recommended.

THOMAS G. HULL, with 14 contributors: *Diseases Transmitted from Animals to Man. Pp. xiii + 403, with 45 figures and 55 tables, Springfield, Illinois and Baltimore, Maryland, Charles C. Thomas, 1941, fabrikoid, $5.50.*

By MAX PINNER

Doctor Hull's monograph seems to be a useful compilation of data pertaining to the topic indicated by its title. It is the second edition of a book first published in 1930 and the Preface states that "All of the chapters of the first edition of the book have been revised and brought up-to-date." This appears to be generally true, but the first chapter, dealing with tuberculosis, presents little evidence of a modern revision. None of the thirty-five references to this chapter, with the exception of one, is of a later date than 1929 and most are considerably older, although a few more recent data are mentioned in the text. This failure of a thorough revision is reflected in the text in which no mention is made of several important contributions during the last decade. Accordingly, exception is taken to a number of statements in this chapter, for example: Johne's bacillus "is not generally considered to be infectious to man." *Mycobacterium stercusis* "is fatal to guinea pigs. . ." "Human adults are resistant to infection with the bovine bacillus. . ." (The whole problem of bovine infection in man is sorely in need of modernization.) "There is a very general agreement throughout the world that practically all infection whether of human or bovine origin, takes place during infancy and childhood."—The table on page 8, showing the relative susceptibility of various animals to human, bovine and avian bacilli, should be thoroughly revised.—The "Chronological Table Showing Incidence of Tubercle Bacilli in Market Milk" ends with 1925.—It is the impression of this reviewer that the other chapters are much more thoroughly "revised and brought up-to-date" than the one on tuberculosis.

The book is attractive, particularly well and pleasingly printed and the typographical details of tables, charts and illustrations are excellent.

Books Received

FRIEDRICH ELLINGER: The Biologic Fundamentals of Radiation Therapy. English Translation by RUEBEN GROSS. Pp. xvi + 360, with 79 illustrations, 1941, Elsevier Publishing Company, Inc., New York, Distributors: Nordeman Publishing Company, Inc., cloth, $5.00.

CARLOS FONSO GANDOLFO AND HUMBERTO R. RUGIERO: Tuberculosis pulmonar. Pp. 535, with 68 roentgenograms, Aniceto Lopez, Buenos Aires, 1941, paper.

GEORG SIMON: Diagnostik und Klinik der Lungentuberkulose des Kindesalters. Pp. 75, with 44 illustrations, 1940, Ferdinand Enke Verlag, Stuttgart, paper, RM 5.

ANNE MARIE SMITH: Play for Convalescent Children in Hospitals and at Home. Pp. xviii + 133, A. S. Barnes and Company, New York, 1941, cloth, $1.60.

AUGUST A. THOMSEN: Doctors Don't Believe It—Why Should You? With introductions by Dr. Logan Clendening and The Right Honorable Lord Horder. Pp. xix + 384, New York, Simon and Schuster, 1941, cloth, $2.50.

JULIUS FRIEDRICH VON FINCK: Die Wirbeltuberkulose und ihre Heilung. Pp. 214, with 122 illustrations, 1940, Ferdinand Enke Verlag, Stuttgart, paper, RM 18.

Papers of Wade Hampton Frost, M.D. A Contribution to Epidemiological Method. Edited by KENNETH F. MAXCY. Pp. viii + 628, 1941, New York, The Commonwealth Fund, cloth, $3.00.

Publicaciones del Centro de Investigaciones Tisiologicas. Director: Prof. Roque A. Izzo. Pp. 411, Pabellon "Las Provincias," Hospital Tornu, Buenos Aires, 1940, paper.

Studies on Tuberculosis. The American Journal of Hygiene Monographic Series, No. 16, February, 1941. Pp. 198, with many tables and charts, Baltimore, The Johns Hopkins Press, 1941, cloth.

AMERICAN TRUDEAU SOCIETY

Report of the Committee on X-ray Apparatus and Technique

Dr. D. O. N. Lindberg, Chairman

Dr. Ezra Bridge
Dr. F. Maurice McPhedran
Dr. Gilberto S. Pesquera
Dr. William H. Weidman
Dr. Homer L. Sampson*
Dr. S. Reid Warren, Jr.*

The Committee has been working during the year 1940–1941 on two major problems:

(1) *The Rôle of Body Section Radiography in Thoracic Diagnoses, Including Technical Considerations.* For the present, only body section apparatus with short focal spot-film distance is being provided by American manufacturers, and the Committee has felt the necessity for fully investigating and evaluating techniques, looking to the enhancement of body section interpretations. Tomography of the chest requires correlation with conventional film methods and advancements. Films from six laboratories equipped with body section radiographic units were demonstrated at the November, 1940 meeting of the Committee in New York City. These techniques varied widely in almost every factor, but it was apparent that the technical quality of the body section film should approximate the standard set for conventional films. The techniques employed by the laboratories were:

	EFFACEMENT	EXCURSION	MA.	TIME	DISTANCE
		inches		*seconds*	*inches*
Laboratory A.....	Spiral	8 (diam.)	10	4	36
Laboratory B.....	Linear	36	20	1	30
Laboratory C.....	Rectilinear (plane)	25	10	3	40
Laboratory D.....	Vertical-Pendulum	12 (hand)	20	4	30
Laboratory E.....	Spiral	4	60	2.5	30
Laboratory F.....	Rectilinear (arc)	42	70	1	60

It was felt that further investigation should include planigraphic studies of the same individual in each of the several laboratories. The selection of a subject was made through the coöperation of Dr. E. S. Mariette, Glen Lake Sanatorium, with due regard being given both the medico-legal and the X-ray exposure factors. These films are being studied by the members of the Committee, and at the time of the fall, 1941, meeting, further conclusions should be available.

Series copy, as practiced by Major Jules Gosselin, Ottawa, Canada, has been considered with the tentative conclusion that its chief value lies in the

* National Tuberculosis Association Members.

estimation of the depth of cavitations already recognized (in Major Gosselin's series) on conventional films, and is a method intended to explore sections of the body with an apparatus of small cost and with the use of four films. It appears to stand as "a compromise procedure, less useful to the chest roentgenologist than tomography."[1] The vernier dialed apparatus appears somewhat complicated and, made originally in France, is not now available directly from the manufacturers.

(2) *Evaluation of Various Methods of Roentgenography of the Chest, Namely, 14″ x 17″ Celluloid, 14″ x 17″ Paper, 4″ x 5″ and 35 mm. Celluloid (Fluorophotography).* A recorded evaluation, similar in form to that of the Air Hygiene study of the comparison of the 14″ x 17″ paper and celluloid roentgenograms, was deemed advisable in view of the increasing interest in the less expensive roentgenological methods. While roentgenologists are agreed, there has existed no clearly defined order of relative diagnostic worth for the guidance of others in the field. Through the courtesy of Dr. Frederick Tice, Chicago Municipal Sanitarium, where all film methods in this particular study were available, a group of patients was filmed by each of the four methods. There were represented in the group: normal lung fields with varying depths of overlying structures; minimal and moderately advanced lesions, including those with peripheral location; lesions of cavitary type; apical pleuritis; adhesions, demonstrable during ineffective stages of induced pneumothorax; childhood tuberculosis. These were sent to the laboratories of each of the members of the Committee for evaluation, and were also reviewed, with evaluations recorded, by a number of chest roentgenologists at the San Antonio meeting. There were 290 judgings of the separate sets of films in the study. In a few instances the 4″ x 5″ and 35 mm. films were not available. The results are as follows:

	FIRST	SECOND	THIRD	FOURTH
14″ x 17″ celluloid	282	6	2	0
14″ x 17″ paper	7	202	63	18
4″ x 5″ celluloid	3	74	134	62
35 mm. celluloid	0	18	84	132

The films were considered for their diagnostic value rather than for any variations of technical quality, because some of these methods are not sufficiently used with strict control of all exposure factors, and must, at present, necessarily stand upon their merits in routine use.

A preliminary observation concerning the 4″ x 10″ fluorophotographic film (4″ x 5″ stereoscopic) suggested its superiority, diagnostically, to all other roentgenographic methods, excepting the familiar and routine 14″ x 17″ celluloid film.

[1] Detailed Report of Committee Meeting, November, 1940.

AMERICAN TRUDEAU SOCIETY

Report of the Committee on Coöperation with the American Board of Internal Medicine

Dr. J. Burns Amberson, Jr., Chairman
Dr. Paul P. McCain Dr. Lewis J. Moorman

More than a year ago discussions were initiated between the American Board of Internal Medicine and the American Trudeau Society (representing the National Tuberculosis Association) concerning the possibility of recognizing in some formal way the subspecialty of Tuberculosis. Similar discussions were held by other groups with reference to the subspecialties. Then the American Board of Internal Medicine developed a plan which was accepted as indicated by the following notice recently issued:

"At the February meetings of the Advisory Board for Medical Specialties and of the Council on Medical Education and Hospitals of the American Medical Association, the proposal of the American Board of Internal Medicine for the recognition of the following subspecialties was approved, Allergy, Cardiovascular Diseases, Gastro-Enterology and Tuberculosis."

The above Committee of the American Trudeau Society has been designated as the Advisory Committee for Tuberculosis by the American Board of Internal Medicine.

A leaflet describing in detail the arrangement for examination and certification is being prepared and will be sent to members of the Society. Other physicians may obtain a copy by applying to the office of the Society, 1790 Broadway, New York City.